

03-26-01

JC14 Rec'd PCT/PTO  
SOV/SEA

22 MAR 2001

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03/22/01

J1057 U.S. PTO

FORM PTO-1390  
(REV. 11-2000)

U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES  
DESIGNATED/ELECTED OFFICE (DO/EO/US)  
CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER

12964.23

U.S. APPLICATION NO. (If known, see 37 CFR 1.5)

09/806080

INTERNATIONAL APPLICATION NO.

PCT/EP99/07055

INTERNATIONAL FILING DATE

22 September 1999

PRIORITY DATE CLAIMED

22 September 1998

TITLE OF INVENTION

GENES OF THE 1-DEOXY D-XYLULOSE BIOSYNTHESIS PATHWAY

APPLICANT(S) FOR DO/EO/US

JOMAA, Hassan

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☒ This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below
4. ☒ The US has been elected by the expiration of 19 months from the priority date (Article 31).
5. ☒ A copy of the International Application as filed (35 U.S.C. 371(c)(2))
  - a. ☐ is attached hereto (required only if not communicated by the International Bureau).
  - b. ☒ has been communicated by the International Bureau.
  - c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☒ An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).
  - a. ☒ is attached hereto.
  - b. ☐ has been previously submitted under 35 U.S.C. 154(d)(4).
7. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
  - a. ☐ are attached hereto (required only if not communicated by the International Bureau).
  - b. ☐ have been communicated by the International Bureau.
  - c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
  - d. ☒ have not been made and will not be made.
8. ☐ An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371 (c)(3)).
9. ☒ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)). unsigned
10. ☒ An English language translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

## Items 11 to 20 below concern document(s) or information included:

11. ☐ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. ☒ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. ☒ A FIRST preliminary amendment.
14. ☐ A SECOND or SUBSEQUENT preliminary amendment.
15. ☐ A substitute specification.
16. ☐ A change of power of attorney and/or address letter.
17. ☒ A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 35 U.S.C. 1.821 - 1.825.
18. ☐ A second copy of the published international application under 35 U.S.C. 154(d)(4).
19. ☐ A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).
20. ☒ Other items or information: Express Mail Certificate  
Post card

U.S. APPLICATION NO. (if known, see 37 CFR 1.53) <b>09480608n</b>	INTERNATIONAL APPLICATION NO. PCT/EP99/07055	ATTORNEY'S DOCKET NUMBER 12964.23
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21. ☒ The following fees are submitted:

**BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)):**

Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO. . . . . **\$1000.00**

International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO . . . . . **\$860.00**

International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO . . . . . **\$710.00**

International preliminary examination fee (37 CFR 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4) . . . . . **\$690.00**

International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4) . . . . . **\$100.00**

**ENTER APPROPRIATE BASIC FEE AMOUNT =**

**CALCULATIONS PTO USE ONLY**

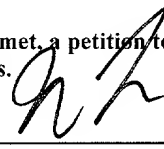
	\$ 860.00	
Surcharge of <b>\$130.00</b> for furnishing the oath or declaration later than <input type="checkbox"/> 20 <input checked="" type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(e)).	\$ 130.00	
<b>CLAIMS</b>	<b>NUMBER FILED</b>	<b>NUMBER EXTRA</b>
Total claims	40 - 20 =	20
Independent claims	8 - 3 =	5
MULTIPLE DEPENDENT CLAIM(S) (if applicable)		+ \$270.00
<b>TOTAL OF ABOVE CALCULATIONS =</b>		\$ 2020.00
<input type="checkbox"/> Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by 1/2.		\$ n/a
<b>SUBTOTAL =</b>		\$ 2020.00
Processing fee of <b>\$130.00</b> for furnishing the English translation later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(f)).		\$ n/a
<b>TOTAL NATIONAL FEE =</b>		\$ 2020.00
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). <b>\$40.00</b> per property +		\$ 40.00
<b>TOTAL FEES ENCLOSED =</b>		\$ 2060.00
		Amount to be refunded: \$
		charged: \$

- a. ☒ A check in the amount of \$ 2060.00 to cover the above fees is enclosed.
- b. ☐ Please charge my Deposit Account No. 08-1394 in the amount of \$ \_\_\_\_\_ to cover the above fees. A duplicate copy of this sheet is enclosed.
- c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 08-1394. A duplicate copy of this sheet is enclosed.
- d. ☐ Fees are to be charged to a credit card. **WARNING:** Information on this form may become public. **Credit card information should not be included on this form.** Provide credit card information and authorization on PTO-2038.

**NOTE:** Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137 (a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO

Warren B. Kice  
 Haynes and Boone, LLP  
 901 Main Street, Suite 3100  
 Dallas, Texas 75202  
 Phone: 214-651-5634  
 Fax: 214-651-5940



\_\_\_\_\_  
 SIGNATURE  
 Warren B. Kice  
 \_\_\_\_\_  
 NAME  
 22,732  
 \_\_\_\_\_  
 REGISTRATION NUMBER

PCT09

## RAW SEQUENCE LISTING

DATE: 04/16/2001

PATENT APPLICATION: US/09/806,080

TIME: 10:33:02

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 7 <130> FILE REFERENCE: 15696  
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 C--> 10 <141> CURRENT FILING DATE: 2001-03-22  
 12 <150> PRIOR APPLICATION NUMBER: DE19923567.8  
 13 <151> PRIOR FILING DATE: 1999-05-22  
 15 <150> PRIOR APPLICATION NUMBER: DE19843279.8  
 16 <151> PRIOR FILING DATE: 1998-09-22  
 18 <160> NUMBER OF SEQ ID NOS: 6  
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 44 aat gat tta gta ata aat aat aca tca aaa tgt gtt tcc att gaa aga 96  
 45 Asn Asp Leu Val Ile Asn Asn Thr Ser Lys Cys Val Ser Ile Glu Arg  
 46 20 25 30  
 48 aga aaa aat aac gca tat ata aat tat ggt ata gga tat aat gga cca 144  
 49 Arg Lys Asn Asn Ala Tyr Ile Asn Tyr Gly Ile Gly Tyr Asn Gly Pro  
 50 35 40 45  
 52 gat aat aaa ata aca aag agt aga aga tgt aaa aga ata aag tta tgc 192  
 53 Asp Asn Lys Ile Thr Lys Ser Arg Arg Cys Lys Arg Ile Lys Leu Cys  
 54 50 55 60  
 56 aaa aag gat tta ata gat att ggt gca ata aag aaa cca att aat gla 240  
 57 Lys Lys Asp Leu Ile Asp Ile Gly Ala Ile Lys Lys Pro Ile Asn Val  
 58 65 70 75 80  
 60 gca att ttt gga agt act ggt agt ata ggt acg aat gct tta aat ata 288  
 61 Ala Ile Phe Gly Ser Thr Gly Ser Ile Gly Thr Asn Ala Leu Asn Ile  
 62 85 90 95  
 64 ata agg gag tgt aat aaa att gaa aat gtt ttt aat gtt aaa gca ttg 336  
 65 Ile Arg Glu Cys Asn Lys Ile Glu Asn Val Phe Asn Val Lys Ala Leu  
 66 100 105 110  
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73 Leu Pro Glu Tyr Leu Cys Ile His Asp Lys Ser Val Tyr Glu Glu Leu  
74 130 135 140  
76 aaa gaa ctg gta aaa aat ata aaa gat tat aaa cct ata ata ttg tgt 480  
77 Lys Glu Leu Val Lys Asn Ile Lys Asp Tyr Lys Pro Ile Ile Leu Cys  
78 145 150 155 160  
80 ggt gat gaa ggg atg aaa gaa ata tgt agt agt aat agt ata gat aaa 528  
81 Gly Asp Glu Gly Met Lys Glu Ile Cys Ser Ser Asn Ser Ile Asp Lys  
82 165 170 175  
84 ata gtt att ggt att gat tct ttt caa gga tta tat tct act atg tat 576  
85 Ile Val Ile Gly Ile Asp Ser Phe Gln Gly Leu Tyr Ser Thr Met Tyr  
86 180 185 190  
88 gca att atg aat aat aaa ata gtt gcg tta gct aat aaa gaa tcc att 624  
89 Ala Ile Met Asn Asn Lys Ile Val Ala Leu Ala Asn Lys Glu Ser Ile  
90 195 200 205  
92 gtc tct gct ggt ttc ttt tta aag aaa tta tta aat att cat aaa aat 672  
93 Val Ser Ala Gly Phe Phe Leu Lys Lys Leu Leu Asn Ile His Lys Asn  
94 210 215 220  
96 gca aag ata ata cct gtt gat tca gaa cat agt gct ata ttt caa tgt 720  
97 Ala Lys Ile Ile Pro Val Asp Ser Glu His Ser Ala Ile Phe Gln Cys  
98 225 230 235 240  
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101 Leu Asp Asn Asn Lys Val Leu Lys Thr Lys Cys Leu Gln Asp Asn Phe  
102 245 250 255  
104 tct aaa att aac aat ata aat aaa ata ttt tta tgt tca tct gga ggt 816  
105 Ser Lys Ile Asn Asn Ile Asn Lys Ile Phe Leu Cys Ser Ser Gly Gly  
106 260 265 270  
108 cca ttt caa aat tta act atg gac gaa tta aaa aat gta aca tca gaa 864  
109 Pro Phe Gln Asn Leu Thr Met Asp Glu Leu Lys Asn Val Thr Ser Glu  
110 275 280 285  
112 aat gct tta aag cat cct aaa tgg aaa atg ggt aag aaa ata act ata 912  
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114 290 295 300  
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122 325 330 335  
124 gaa tgc att ata cal tct tgt gll gaa ttt ata gac aaa lca gla ata 1056  
125 Glu Cys Ile Ile His Ser Cys Val Glu Phe Ile Asp Lys Ser Val Ile  
126 340 345 350  
128 agt caa atg tat tat cca gat atg caa ata ccc ata tta tat tct tta 1104  
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130 355 360 365  
132 aca tgg cct gat aga ata aaa aca aat tta aaa cct tta gat ttg gct 1152  
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## RAW SEQUENCE LISTING

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138 385      390      395      400
140 tgt att aaa tta gct tat caa gca ggt ata aaa gga aac ttt tat cca 1248
141 Cys Ile Lys Leu Ala Tyr Gln Ala Gly Ile Lys Gly Asn Phe Tyr Pro
142      405      410      415
144 act gta cta aat gcg tca aat gaa ata gct aac aac tta ttt ttg aat 1296
145 Thr Val Leu Asn Ala Ser Asn Glu Ile Ala Asn Asn Leu Phe Leu Asn
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148 aat aaa att aaa tat ttt gat att tcc tct ata ata tcg caa gtt ctt 1344
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150      435      440      445
152 gaa tct ttc aat tct caa aag gtt tcg gaa aat agt gaa gat tta atg 1392
153 Glu Ser Phe Asn Ser Gln Lys Val Ser Glu Asn Ser Glu Asp Leu Met
154      450      455      460
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175 20 25 30
177 Arg Lys Asn Asn Ala Tyr Ile Asn Tyr Gly Ile Gly Tyr Asn Gly Pro
178 35 40 45
180 Asp Asn Lys Ile Thr Lys Ser Arg Arg Cys Lys Arg Ile Lys Leu Cys
181 50 55 60
183 Lys Lys Asp Leu Ile Asp Ile Gly Ala Ile Lys Lys Pro Ile Asn Val
184 65 70 75 80
186 Ala Ile Phe Gly Ser Thr Gly Ser Ile Gly Thr Asn Ala Leu Asn Ile
187 85 90 95
189 Ile Arg Glu Cys Asn Lys Ile Glu Asn Val Phe Asn Val Lys Ala Leu
190 100 105 110
192 Tyr Val Asn Lys Ser Val Asn Glu Leu Tyr Glu Gln Ala Arg Glu Phe
193 115 120 125
195 Leu Pro Glu Tyr Leu Cys Ile His Asp Lys Ser Val Tyr Glu Glu Leu
196 130 135 140
198 Lys Glu Leu Val Lys Asn Ile Lys Asp Tyr Lys Pro Ile Ile Leu Cys
199 145 150 155 160
201 Gly Asp Glu Gly Met Lys Glu Ile Cys Ser Ser Asn Ser Ile Asp Lys
202 165 170 175

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## RAW SEQUENCE LISTING

DATE: 04/16/2001

PATENT APPLICATION: US/09/806,080

TIME: 10:33:02

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210 Val Ser Ala Gly Phe Phe Leu Lys Lys Leu Leu Asn Ile His Lys Asn
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214 225             230             235             240
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234 Glu Cys Ile Ile His Ser Cys Val Glu Phe Ile Asp Lys Ser Val Ile
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255 Glu Ser Phe Asn Ser Gln Lys Val Ser Glu Asn Ser Glu Asp Leu Met
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## RAW SEQUENCE LISTING

DATE: 04/16/2001

PATENT APPLICATION: US/09/806,080

TIME: 10:33:02

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288 tatca atg att ttt aat tat gtg ttt ttt aag aac ttt gta cca gtt gtt 170
289 Met Ile Phe Asn Tyr Val Phe Phe Lys Asn Phe Val Pro Val Val
290      1          5          10          15
292 cta tac att ctg ctt ata ata tat att aac tta aat ggc atg aat aat 218
293 Leu Tyr Ile Leu Leu Ile Ile Tyr Ile Asn Leu Asn Gly Met Asn Asn
294      20          25          30
296 aaa aat caa ata aaa aca gaa aaa att tat ata aag aaa ttg aat agg 266
297 Lys Asn Gln Ile Lys Thr Glu Lys Ile Tyr Ile Lys Lys Leu Asn Arg
298      35          40          45
300 ttg tca agg aaa aat tgg tta tgt agt tct aaa aat aaa ata gca tgc 314
301 Leu Ser Arg Lys Asn Ser Leu Cys Ser Ser Lys Asn Lys Ile Ala Cys
302      50          55          60
304 ttg ttc gal ala gga aat gal gal aat aga aat acg aca tal ggc tal 362
305 Leu Phe Asp Ile Gly Asn Asp Asp Asn Arg Asn Thr Thr Tyr Gly Tyr
306      65          70          75
308 aat gtg aat gct aaa aat gat gat att aat tcc tta cta aaa aat aat 410
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314      100         105         110
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317 Ile Ser Thr Asn Lys Ile Ser Gly Ser Ile Ser Asn Ile Cys Ser Arg
318      115         120         125
320 aat caa aaa gaa aat gaa caa aaa aga aat aaa caa aga tgt tta act 554
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334      180         185         190
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342      210         215         220

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VERIFICATION SUMMARY

DATE: 04/16/2001

PATENT APPLICATION: US/09/806,080

TIME: 10:33:04

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L:9 M:270 C: Current Application Number differs, Replaced Current Application Number  
L:10 M:271 C: Current Filing Date differs, Replaced Current Filing Date

0906080-000101



PCT

## RAW SEQUENCE LISTING

DATE: 04/04/2001

PATENT APPLICATION: US/09/806,080

TIME: 11:20:05

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 7 <130> FILE REFERENCE: 15696  
 C--> 9 <140> CURRENT APPLICATION NUMBER: US/09/806,080  
 C--> 10 <141> CURRENT FILING DATE: 2001-03-22  
 12 <150> PRIOR APPLICATION NUMBER: DE19923567.8  
 13 <151> PRIOR FILING DATE: 1999-05-22  
 15 <150> PRIOR APPLICATION NUMBER: DE19843279.8  
 16 <151> PRIOR FILING DATE: 1998-09-22  
 18 <160> NUMBER OF SEQ ID NOS: 6  
 20 <170> SOFTWARE: PatentIn Ver. 2.1

Does Not Comply  
 Corrected Diskette Needed  
 See p. 4

## ERRORED SEQUENCES

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 606 Tyr Ile Leu Leu Ile Ile Tyr Ile Asn Leu Asn Gly Met Asn Asn Lys  
 607 20 25 30  
 609 Asn Gln Ile Lys Thr Glu Lys Ile Tyr Ile Lys Lys Leu Asn Arg Leu  
 610 35 40 45  
 612 Ser Arg Lys Asn Ser Leu Cys Ser Ser Lys Asn Lys Ile Ala Cys Leu  
 613 50 55 60  
 615 Phe Asp Ile Gly Asn Asp Asp Asn Arg Asn Thr Thr Tyr Gly Tyr Asn  
 616 65 70 75 80  
 618 Val Asn Val Lys Asn Asp Asp Ile Asn Ser Leu Leu Lys Asn Asn Tyr  
 619 85 90 95  
 621 Ser Asn Lys Leu Tyr Met Asp Lys Arg Lys Asn Ile Asn Asn Val Ile  
 622 100 105 110  
 624 Ser Thr Asn Lys Ile Ser Gly Ser Ile Ser Asn Ile Cys Ser Arg Asn  
 625 115 120 125  
 627 Gln Lys Glu Asn Glu Gln Lys Arg Asn Lys Gln Arg Cys Leu Thr Gln  
 628 130 135 140  
 630 Cys His Thr Tyr Asn Met Ser His Glu Gln Asp Lys Leu Ala Asn Asp  
 631 145 150 155 160  
 633 Asn Asn Arg Asn Asn Lys Lys Asn Phe Asn Leu Leu Phe Ile Asn Tyr  
 634 165 170 175  
 636 Phe Asn Leu Lys Arg Met Lys Asn Ser Leu Leu Asn Lys Asp Asn Phe  
 637 180 185 190  
 639 Phe Tyr Cys Lys Glu Lys Lys Leu Ser Phe Leu His Lys Ala Tyr Lys  
 640 195 200 205

## RAW SEQUENCE LISTING

DATE: 04/04/2001

PATENT APPLICATION: US/09/806,080

TIME: 11:20:06

Input Set : A:\S0109991.app

Output Set: N:\CRF3\04042001\I806080.raw

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642 Lys Lys Asn Cys Thr Phe Gln Asn Tyr Ser Leu Lys Arg Lys Ser Asn
643      210      215      220
645 Arg Asp Ser His Lys Leu Phe Ser Gly Glu Phe Asp Asp Tyr Thr Asn
646 225      230      235      240
648 Asn Asn Ala Leu Tyr Glu Ser Glu Lys Lys Glu Tyr Ile Thr Leu Asn
649      245      250      255
651 Asn Asn Asn Lys Asn Asn Asn Asn Lys Asn Asn Asp Asn Lys Asn Asn
652      260      265      270
654 Asp Asn Asn Asp Tyr Asn Asn Asn Asn Ser Cys Asn Asn Leu Gly Glu
655      275      280      285
657 Arg Ser Asn His Tyr Asp Asn Tyr Gly Gly Asp Asn Asn Asn Pro Cys
658 290      295      300
660 Asn Asn Asn Asn Asp Lys Tyr Asp Ile Gly Lys Tyr Phe Lys Gln Ile
661 305      310      315      320
663 Asn Thr Phe Ile Asn Ile Asp Glu Tyr Lys Thr Ile Tyr Gly Asp Glu
664      325      330      335
666 Ile Tyr Lys Glu Ile Tyr Glu Leu Tyr Val Glu Arg Asn Ile Pro Glu
667      340      345      350
669 Tyr Tyr Glu Arg Lys Tyr Phe Ser Glu Asp Ile Lys Lys Ser Val Leu
670      355      360      365
672 Phe Asp Ile Asp Lys Tyr Asn Asp Val Glu Phe Glu Lys Ala Ile Lys
673      370      375      380
675 Glu Glu Phe Ile Asn Asn Gly Val Tyr Ile Asn Asn Ile Asp Asn Thr
676 385      390      395      400
678 Tyr Tyr Lys Lys Glu Asn Ile Leu Ile Met Lys Lys Ile Leu His Tyr
679      405      410      415
681 Phe Pro Leu Leu Lys Leu Ile Asn Asn Pro Ser Asp Leu Lys Lys Leu
682      420      425      430
684 Lys Lys Gln Tyr Leu Pro Leu Leu Ala His Glu Leu Lys Ile Phe Leu
685      435      440      445
687 Phe Phe Ile Val Asn Ile Thr Gly Gly His Phe Ser Ser Val Leu Ser
688      450      455      460
690 Ser Leu Glu Ile Gln Leu Leu Leu Tyr Ile Phe Asn Gln Pro Tyr
691 465      470      475      480
693 Asp Asn Val Ile Tyr Asp Ile Gly His Gln Ala Tyr Val His Lys Ile
694      485      490      495
696 Leu Thr Gly Arg Lys Leu Leu Phe Leu Ser Leu Arg Asn Lys Lys Gly
697      500      505      510
699 Ile Ser Gly Phe Leu Asn Ile Phe Glu Ser Ile Tyr Asp Lys Phe Gly
700      515      520      525
702 Ala Gly His Ser Ser Thr Ser Leu Ser Ala Ile Gln Gly Tyr Tyr Glu
703      530      535      540
705 Ala Glu Trp Gln Val Lys Asn Lys Glu Lys Tyr Gly Asn Gly Asp Ile
706 545      550      555      560
708 Glu Ile Ser Asp Asn Ala Asn Val Thr Asn Asn Glu Arg Ile Phe Gln
709      565      570      575
711 Lys Gly Ile His Asn Asp Asn Asn Ile Asn Asn Asn Ile Asn Asn Asn
712      580      585      590
714 Asn Tyr Ile Asn Pro Ser Asp Val Val Gly Arg Glu Asn Thr Asn Val

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## RAW SEQUENCE LISTING

DATE: 04/04/2001

PATENT APPLICATION: US/09/806,080

TIME: 11:20:06

Input Set : A:\S0109991.app

Output Set: N:\CRF3\04042001\I806080.raw

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715          595          600          605
717 Pro Asn Val Arg Asn Asp Asn His Asn Val Asp Lys Val His Ile Ala
718          610          615          620
720 Ile Ile Gly Asp Gly Gly Leu Thr Gly Gly Met Ala Leu Glu Ala Leu
721 625          630          635          640
723 Asn Tyr Ile Ser Phe Leu Asn Ser Lys Ile Leu Ile Ile Tyr Asn Asp
724          645          650          655
726 Asn Gly Gln Val Ser Leu Pro Thr Asn Ala Val Ser Ile Ser Gly Asn
727          660          665          670
729 Arg Pro Ile Gly Ser Ile Ser Asp His Leu His Tyr Phe Val Ser Asn
730          675          680          685
732 Ile Glu Ala Asn Ala Gly Asp Asn Lys Leu Ser Lys Asn Ala Lys Glu
733          690          695          700
735 Asn Asn Ile Phe Glu Asn Leu Asn Tyr Asp Tyr Ile Gly Val Val Asn
736 705          710          715          720
738 Gly Asn Asn Thr Glu Glu Leu Phe Lys Val Leu Asn Asn Ile Lys Glu
739          725          730          735
741 Asn Lys Leu Lys Arg Ala Thr Val Leu His Val Arg Thr Lys Lys Ser
742          740          745          750
744 Asn Asp Phe Ile Asn Ser Lys Ser Pro Ile Ser Ile Leu His Ser Ile
745          755          760          765
747 Lys Lys Asn Glu Ile Phe Pro Phe Asp Thr Thr Ile Leu Asn Gly Asn
748          770          775          780
750 Ile His Lys Glu Asn Lys Ile Glu Glu Glu Lys Asn Val Ser Ser Ser
751 785          790          795          800
753 Thr Lys Tyr Asp Val Asn Asn Lys Asn Asn Lys Asn Asn Asp Asn Ser
754          805          810          815
756 Glu Ile Ile Lys Tyr Glu Asp Met Phe Ser Lys Glu Thr Phe Thr Asp
757          820          825          830
759 Ile Tyr Thr Asn Glu Met Leu Lys Tyr Leu Lys Lys Asp Arg Asn Ile
760          835          840          845
762 Ile Phe Leu Ser Pro Ala Met Leu Gly Gly Ser Gly Leu Val Lys Ile
763          850          855          860
765 Ser Glu Arg Tyr Pro Asn Asn Val Tyr Asp Val Gly Ile Ala Glu Gln
766 865          870          875          880
768 His Ser Val Thr Phe Ala Ala Ala Met Ala Met Asn Lys Lys Leu Lys
769          885          890          895
771 Ile Gln Leu Cys Ile Tyr Ser Thr Phe Leu Gln Arg Ala Tyr Asp Gln
772          900          905          910
774 Ile Ile His Asp Leu Asn Leu Gln Asn Ile Pro Leu Lys Val Ile Ile
775          915          920          925
777 Gly Arg Ser Gly Leu Val Gly Glu Asp Gly Ala Thr His Gln Gly Ile
778          930          935          940
780 Tyr Asp Leu Ser Tyr Leu Gly Thr Leu Asn Asn Ala Tyr Ile Ile Ser
781 945          950          955          960
783 Pro Ser Asn Gln Val Asp Leu Lys Arg Ala Leu Arg Phe Ala Tyr Leu
784          965          970          975
786 Asp Lys Asp His Ser Val Tyr Ile Arg Ile Pro Arg Met Asn Ile Leu
787          980          985          990

```

## RAW SEQUENCE LISTING

DATE: 04/04/2001

PATENT APPLICATION: US/09/806,080

TIME: 11:20:06

Input Set : A:\S0109991.app

Output Set: N:\CRF3\04042001\I806080.raw

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789 Ser Asp Lys Tyr Met Lys Gly Tyr Leu Asn Ile His Met Lys Asn Glu
790      995      1000      1005
792 Ser Lys Asn Ile Asp Val Asn Val Asp Ile Asn Asp Asp Val Asp Lys
793      1010      1015      1020
795 Tyr Ser Glu Glu Tyr Met Asp Asp Asp Asn Phe Ile Lys Ser Phe Ile
E--> 796 025      1030      1035      1040
798 Gly Lys Ser Arg Ile Ile Lys Met Asp Asn Glu Asn Asn Asn Thr Asn
799      1045      1050      1055
801 Glu His Tyr Ser Ser Arg Gly Asp Thr Gln Thr Lys Lys Lys Lys Val
802      1060      1065      1070
804 Cys Ile Phe Asn Met Gly Ser Met Leu Phe Asn Val Ile Asn Ala Ile
805      1075      1080      1085
807 Lys Glu Ile Glu Lys Glu Gln Tyr Ile Ser His Asn Tyr Ser Phe Ser
808      1090      1095      1100
810 Ile Val Asp Met Ile Phe Leu Asn Pro Leu Asp Lys Asn Met Ile Asp
E--> 811 105      1110      1115      1120
813 His Val Ile Lys Gln Asn Lys His Gln Tyr Leu Ile Thr Tyr Glu Asp
814      1125      1130      1135
816 Asn Thr Ile Gly Gly Phe Ser Thr His Phe Asn Asn Tyr Leu Ile Glu
817      1140      1145      1150
819 Asn Asn Tyr Ile Thr Lys His Asn Leu Tyr Val His Asn Ile Tyr Leu
820      1155      1160      1165
822 Ser Asn Glu Pro Ile Glu His Ala Ser Phe Lys Asp Gln Gln Glu Val
823      1170      1175      1180
825 Val Lys Met Asp Lys Cys Ser Leu Val Asn Arg Ile Lys Asn Tyr Leu
E--> 826 185      1190      1195      1200
828 Lys Asn Asn Pro Thr
829      1205

```

*Invalid amino acid numbers.  
Move numbers circled one space  
to the right as shown below.*

*Tyr  
1 0 2 5*

*Ile  
1 1 0 5*

*Val  
1 1 8 5*

## VERIFICATION SUMMARY

DATE: 04/04/2001

PATENT APPLICATION: US/09/806,080

TIME: 11:20:07

Input Set : A:\S0109991.app

Output Set: N:\CRF3\04042001\I806080.raw

L:1 M:259 W: Allowed number of lines exceeded, (1) GENERAL INFORMATION:  
L:9 M:270 C: Current Application Number differs, Replaced Current Application Number  
L:10 M:271 C: Current Filing Date differs, Replaced Current Filing Date  
L:796 M:332 E: (32) Invalid/Missing Amino Acid Numbering, SEQ ID:4  
M:332, Repeated in SeqNo=4

09/806080

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:  
Jomaa

Serial No.: United States National Phase  
of PCT/EP99/07055

Filed: Herewith

For: GENES OF THE 1-DEOXY  
D-XYLULOSE BIOSYNTHESIS  
PATHWAY

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§

Attorney Docket No.: 12964.23

I. A. Filing Date: 22 SEP1999

Priority Date: 22 SEP 1998

Attention: DO/EO/US  
Commissioner For Patents  
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Dear Sir:

Prior to the initial examination of the above-identified application, please amend the application as follows:

IN THE CLAIMS:

6. (Amended) Process for the production of transgenic viruses, eukaryotes and prokaryotes for modifying the isoprenoid content, characterized in that a DNA sequence according to claim 4 is transferred and incorporated into the genome of viruses, eukaryotic and prokaryotic cells with or without use of a vector.

7. (Amended) Transgenic systems, in particular plants and plant cells which contain one or more DNA sequences according to one of claims 1 to 3 as "foreign" or "additional" DNA, which sequences are expressed.

8. (Amended) Expression vector containing one or more DNA sequences according to one of claims 1 to 3.

11. (Amended) Protein according to claim 9, characterized in that it a) is the product of viral, prokaryotic or eukaryotic expression of exogenous DNA, b) is coded by sequences SEQ ID no. 1, 3 or 5 or is coded by DNA sequences which hybridize with DNA sequences SEQ ID no. 1, 3, 5 or fragments of these DNA sequences in the DNA region which codes for the mature protein, or c) is coded by DNA sequences which would hybridize without degeneration of the genetic code with the sequences defined in b) and which code for a polypeptide with a corresponding amino acid sequence.

12. (Amended) Protein according to one of claims 1-3, 6, 9, 10, 11, 22 and 23 characterized in that it comprises the amino acid sequences SEQ ID no. 2, 4 or 6.

18. (Amended) Use of DNA according to one of claims 1 to 3.

Please add the following Claims 19-23.

19. Use of proteins according to claim 9.

20. Use of proteins according to Claim 10.

21. Use of transgenic systems according to claim 7 for the prevention or treatment of diseases in humans and animals.

22. Process for the production of transgenic viruses, eukaryotes and prokaryotes for modifying the isoprenoid content, characterized in that a DNA sequence according to claim 5 is transferred and incorporated into the genome of viruses, eukaryotic and prokaryotic cells with or without use of a vector.

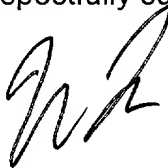
23. Protein according to claim 10, characterized in that it a) is the product of viral, prokaryotic or eukaryotic expression of exogenous DNA, b) is coded by sequences SEQ ID no. 1, 3 or 5 or is coded by DNA sequences which hybridize with DNA sequences SEQ ID no. 1, 3, 5 or fragments of these DNA sequences in the DNA region which codes for the mature protein, or c) is coded by DNA sequences which would hybridize without degeneration of the genetic code with the sequences defined in b) and which code for a polypeptide with a corresponding amino acid sequence.

REMARKS

Claims 1-23 remain in the application. Claims 6, 7, 8, 11, 12 and 18 have been amended. Claims 19-23 have been added. The filing fee has been calculated according to the above-amendments.

Should the Examiner have any questions or comments regarding the amendments, the Examiner is invited to telephone the undersigned at the number listed below.

Respectfully submitted,



Warren B. Kice  
Registration No. 22,732

Dated: 3/22/01  
HAYNES AND BOONE, L.L.P.  
901 Main Street, Suite 3100  
Dallas, Texas 75202-3789  
Telephone: 214/651-5634  
Fax: 214/651-5940  
Docket Number: 12964.23  
D-880233.1


EXPRESS MAIL NO.: EL418590374US

DATE OF DEPOSIT: March 22, 2001

This paper and fee are being deposited with the U.S. Postal Service Express Mail Post Office to Addressee service under 37 CFR §1.10 on the date indicated above and is addressed to the Commissioner for Patents, Washington, D.C. 20231

**SANDRA KUBIN**

Name of person mailing paper and fee



Signature of person mailing paper and fee



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	§	
Jomaa	§	Attorney Docket No.: 12964.23
	§	
Serial No.: United States National Phase	§	I. A. Filing Date: 22 SEP1999
of PCT/EP99/07055	§	
	§	
Filed: Herewith	§	Priority Date: 22 SEP 1998
	§	
For: GENES OF THE 1-DEOXY	§	
D-XYLULOSE BIOSYNTHESIS	§	
PATHWAY	§	

Attention: DO/EO/US  
Commissioner For Patents  
Washington, D.C. 20231

REDLINE VERSION FOR PRELIMINARY AMENDMENT

6. (Amended) Process for the production of transgenic viruses, eukaryotes and prokaryotes for modifying the isoprenoid content, [~~characterised~~] characterized in that a DNA sequence according to claim 4 [or 5] is transferred and incorporated into the genome of viruses, eukaryotic and prokaryotic cells with or without use of a vector.
7. (Amended) Transgenic systems, in particular plants and plant cells which contain one or more DNA sequences according to one of claims 1 to [5]3 as "foreign" or "additional" DNA, which sequences are expressed.
8. (Amended) Expression vector containing one or more DNA sequences according to one of claims 1 to [5] 3.
11. (Amended) Protein according to [one of] claim[s] 9 [and 10], [~~characterised~~] characterized in that it a) is the product of viral, prokaryotic or eukaryotic expression of exogenous DNA, b) is coded by sequences SEQ ID no. 1, 3 or 5 or is coded by DNA sequences which [~~hybridise~~] hybridize with DNA sequences SEQ ID no. 1, 3, 5 or fragments of these DNA sequences in the DNA region which codes for the mature protein, or c) is coded by DNA sequences which would [~~hybridise~~] hybridize without degeneration of the genetic code with the sequences defined in b) and which code for a polypeptide with a corresponding amino acid sequence.
12. (Amended) Protein according to one of [the preceding] claims 1-3, 6, 9, 10, 11, 22 and 23 [~~characterised~~] characterized in that it comprises the amino acid sequences SEQ ID no. 2, 4 or 6.

18. (Amended) Use of DNA according to one of claims 1 to [5] 3. [or of proteins according to one of claims 9 to 12 or of transgenic systems according to claim 7 for the prevention or treatment of diseases in humans and animals.]

09/806080  
PTO/PCT Rec'd 01 JUN 2001

PATENT/DOCKET 12964.23

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:  
Hassan Jomaa

Serial No.: 09/806,080

Filed: March 22, 2001

For: GENES OF THE 1-DEOXY D-XYLULOSE BIOSYNTHESIS PATHWAY

§  
§  
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§  
§  
§  
§

I. A. Filing Date: 22 SEP 1999

Priority Date: 22 SEP 1998

Attention: DO/EO/US  
Box PCT  
Commissioner for Patents  
Washington, D.C. 20231

RESPONSE TO COMPLY WITH REQUIREMENTS FOR SEQUENCE DISCLOSURES

Sir:

The information recorded in computer readable form (diskette sent with original filing on 22 March 2001) is identical to the written sequence listing.

We believe this response to complete the requirements under 35 U.S.C. 371.

Respectfully submitted,



Warren B. Kice  
Reg. No. 22,732

Dated: 5/29/01  
HAYNES AND BOONE, L.P.  
901 Main Street, Suite 3100  
Dallas, Texas 75202-3789  
Telephone: 214/651-5634  
Fax: 214/651-5940  
Docket Number: 12964.23

D-900261.1

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner For Patents, Box PCT, Washington, D.C. 20231

on

May 29, 2001  
Sandra Kubin  
SANDRA KUBIN

Genes of the 1-deoxy-D-xylulose biosynthesis pathway

The present invention relates to DNA sequences which, when incorporated into the genome of viruses, eukaryotes and prokaryotes, modify isoprenoid biosynthesis and to a genetic engineering process for the production of these transgenic viruses, eukaryotes and prokaryotes. The invention also relates to a process for the identification of substances having herbicidal, antimicrobial, antiparasitic, antiviral, fungicidal, bactericidal action in plants and antimicrobial, antiparasitic, antimycotic, antibacterial and antiviral action in humans and animals.

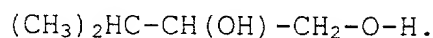
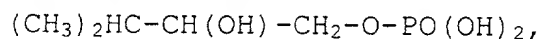
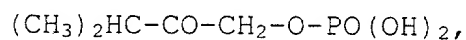
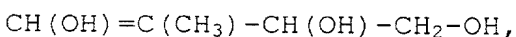
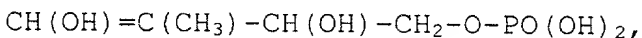
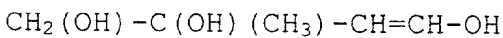
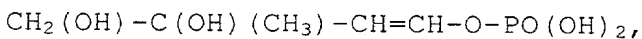
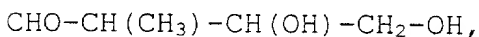
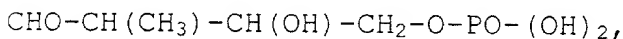
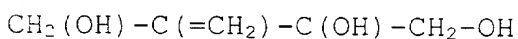
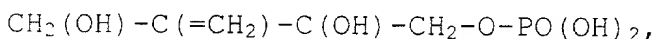
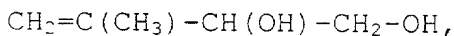
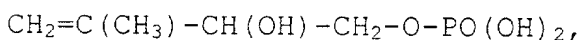
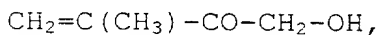
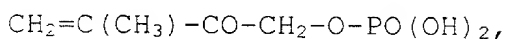
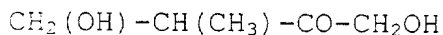
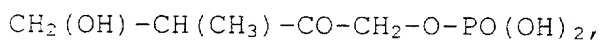
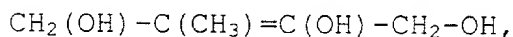
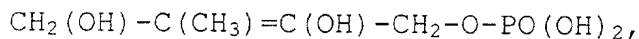
The biosynthesis pathway for the formation of isoprenoids via the classical acetate/mevalonate pathway and an alternative mevalonate-independent biosynthesis pathway, the deoxy-D-xylulose phosphate pathway is already known (Rohmer, M., Knani, M., Simonin, P., Sutter, B. and Sahm, H. (1993): *Biochem. J.* 295: 517-524).

It is, however, not known how and by which pathways it is possible to bring about a change in the isoprenoid concentration in viruses, eukaryotes and prokaryotes by means of the deoxy-D-xylulose phosphate pathway. Figure 1 shows this biosynthesis pathway.

DNA sequences are consequently provided which code for 1-deoxy-D-xylulase 5-phosphate synthase (DOXP synthase), 1-deoxy-D-xylulose 5-phosphate reductoisomerase (DOXP reductoisomerase) or the *gcpE* protein. All three genes and enzymes are involved in isoprenoid biosynthesis.

(Translator's comment: The portion at the beginning of the next paragraph enclosed in square brackets corresponds to the beginning of the sentence which finishes on page 2, line 1 of the original).

[The gcpE protein has a kinase function and catalyses the phosphorylation of a sugar or a phosphorus sugar or a precursor of isoprenoid biosynthesis, in particular the phosphorylation of 2-C-methyl-D-erythritol, 2-C-methyl-D-erytritol phosphate, in particular 2-C-methyl-D-erythritol 4-phosphate, 2-C-methyl-D-erythrose, 2-C-methyl-D-erythrose] phosphate, in particular 2-C-methyl-D-erythrose 4-phosphate. In the precursor of isoprenoid synthesis, the gcpE protein in particular catalyses the phosphorylation of the following substances:



DOXP synthase catalyses the condensation of pyruvate and  
glyceraldehyde 3-phosphate to yield 1-deoxy-D-xylulose  
5-phosphate and DOXP reductoisomerase catalyses the  
5 conversion of 1-deoxy-D-xylulose 5-phosphate into  
2-C-methyl-D-erythritol 4-phosphate (*c.f.* Fig. 1).

The invention relates to the following DNA sequences:  
DNA sequences which code for a polypeptide with the amino  
10 acid sequence shown in SEQ ID no. 2 or for an analogue or  
derivative of the polypeptide according to SEQ ID no. 2,  
in which one or more amino acids have been deleted, added  
or replaced by other amino acids, wherein the enzymatic  
action of the polypeptide is retained, and which  
15 sequences originate from parasites, wherein sequence  
variations occurring within the framework of natural  
strain variability are included,

DNA sequences which code for a polypeptide with the amino  
20 acid sequence shown in SEQ ID no. 4 or for an analogue or  
derivative of the polypeptide according to SEQ ID no. 4,  
in which one or more amino acids have been deleted, added  
or replaced by other amino acids, wherein the enzymatic  
action of the polypeptide is retained, and which  
25 sequences originate from parasites, wherein sequence  
variations occurring within the framework of natural  
strain variability are included,

and DNA sequences which code for a polypeptide with the  
30 amino acid sequence shown in SEQ ID no. 6 or for an  
analogue or derivative of the polypeptide according to  
SEQ ID no. 6, in which one or more amino acids have been

deleted, added or replaced by other amino acids, wherein the catalytic function of the polypeptide is retained.

5 The genes and the gene products thereof (polypeptides) are shown with their primary structure and are assigned as follows:

SEQ ID no. 1: 1-deoxy-D-xylulose 5-phosphate reducto-  
isomerase gene

10 SEQ ID no. 2: 1-deoxy-D-xylulose 5-phosphate reducto-  
isomerase

SEQ ID no. 3: 1-deoxy-D-xylulose 5-phosphate synthase  
gene

SEQ ID no. 4: 1-deoxy-D-xylulose 5-phosphate synthase

09006080 060101

- 4 -

SEQ ID no. 5: gcpE gene

SEQ ID no. 6: gcpE proteins.

5 The DNA sequences all originate from *Plasmodium falciparum*.

10 Apart from the DNA sequences stated in the sequence listing, suitable sequences are also those which, as a result of the degeneration of the genetic code, have another DNA sequence, but code for the same peptide or for an analogue or derivative of the polypeptide, in which one or more amino acids have been deleted, added or replaced by other amino acids.

15 The sequences according to the invention are suitable for the expression of genes in viruses, eukaryotes and prokaryotes which are responsible for isoprenoid biosynthesis in the 1-deoxy-D-xylulose pathway.

20 According to the invention, eukaryotes or eukaryotic cells include animal cells, plant cells, algae, yeasts, fungi, while prokaryotes or prokaryotic cells include bacteria, archaebacteria and eubacteria.

25 When a DNA sequence is incorporated into a genome on which the above-stated DNA sequence is located, expression of the above-described genes in viruses, eukaryotes and prokaryotes is enabled. The viruses, eukaryotes and prokaryotes transformed according to the invention are cultivated in a manner known per se and the isoprenoid formed during such cultivation is isolated and optionally purified. Not all isoprenoids need to be

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- 5 -

isolated as in some case the isoprenoids are released directly into the ambient air.

The invention furthermore relates to a process for the production of transgenic viruses, eukaryotes and prokaryotes in order to modify the isoprenoid content, which process comprises the following steps.

- a) Production of a DNA sequence with the following sub-sequences
  - i) promoter which is active in viruses, eukaryotes and prokaryotes and ensures the formation of an RNA in the intended target tissue or target cells,
  - ii) DNA sequence which codes for a polypeptide with the amino acid sequence shown in SEQ ID no. 2, 4 or 6 or for an analogue or derivative of the polypeptide according to SEQ ID no. 2, 4 or 6,
  - iii) 5' and 3' untranslated sequence which enables or enhances expression of the stated genes in viruses, eukaryotes and prokaryotes,
- b) transfer and incorporation of the DNA sequence into the genome of viruses, prokaryotic or eukaryotic cells with or without the use of a vector (for example plasmid, viral DNA).

The intact, whole plants may be regenerated from plant cells transformed in this manner.

The protein-coding sequences with the nucleotide sequences SEQ ID no. 1, SEQ ID no. 3 and SEQ ID no. 5 may be provided with a promoter which ensures transcription in certain organs or cells, which promoter is coupled in

- 6 -

sense orientation (3' end of the promoter to the 5' end of the coding sequence) to the sequence which codes the protein to be formed. A termination signal which determines termination of mRNA synthesis is attached to the 3' end of the coding sequence. In order to direct the protein which is to be expressed to certain subcellular compartments, such as chloroplasts, amyloplasts, mitochondria, vacuoles, cytosol or intercellular spaces, a further sequence which codes for a so-called signal sequence or a transit peptide may be inserted between the promoter and the coding sequence. In some cases, it is necessary to insert sequences which code for a signal at the COOH terminus of the protein. The sequence must be in the same reading frame as the coding sequence of the protein. A large number of cloning vectors is available in order to prepare for the introduction of the DNA sequences according to the invention into higher plants, which vectors contain a replication signal for *E. coli* and a marker which permits selection of the transformed cells. Depending upon the method by which desired genes are introduced into the plant, further DNA sequences may be required. If, for example, the Ti or Ri plasmid is used to transform the plant cells, at least one right border, but frequently the right border and left border of the Ti and Ri plasmid T-DNA must be inserted as a flanking region into the genes to be introduced. The use of T-DNA for transforming plant cells has been intensively investigated and comprehensively described in EP 120516; Hoekama in "The Binary Plant Vector System", Offset-drukkerij Kanters B.V. Alblasterdam (1985), chapter V; Fraley et al., *Crit.Rev.Plant Sci.* 4, 1-46 and An et al. (1985) *EMBO J.* 4, 277-287. Once the introduced DNA has been incorporated into the genome, it is

- 7 -

generally stable and is also retained in the descendants of the originally transformed cells. It normally contains a selection marker, which imparts to the transformed plant cells resistance to a biocide or an antibiotic, such as kanamycin, G 418, bleomycin, hygromycin or phosphinotricin and others. The particular marker used is thus intended to allow selection of transformed cells from cells lacking the inserted DNA.

Many techniques are available for introducing DNA into a plant. These techniques include transformation with the assistance of agrobacteria, for example *Agrobacterium tumefaciens*, protoplast fusion, microinjection of DNA, electroporation, as well as ballistic methods and virus infection. Whole plants may then be regenerated from the transformed plant material in a suitable medium which may contain antibiotics or biocides for selection purposes. No particular requirements are placed upon the plasmids for injection and electroporation. However, if whole plants are to be regenerated from such transformed cells, a selectable marker gene must be present. The transformed cells grow in the plants in the conventional manner (McCormick et al. (1986), *Plant Cell Reports* 5, 81-84). The plants may be cultivated normally and be crossed with plants which have the same transformed genome or other genomes. The resultant individuals have the corresponding phenotypic properties.

The present invention also provides expression vectors which contain one or more of the DNA sequences according to the invention. Such expression vectors are obtained by providing the DNA sequences according to the invention with suitable functional regulation signals. Such

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regulation signals are DNA sequences which are responsible for expression, for example promoters, operators, enhancers, ribosomal binding sites, and are recognised by the host organism.

5

Further regulation signals, which for example control replication or recombination of the recombinant DNA in the host organism, may optionally also be a constituent part of the expression vector.

10

The host organisms transformed with the DNA sequences or expression vectors according to the invention are also provided by the present invention.

15

Suitable host cells and organisms for expressing the enzymes according to the invention are those which comprise no intrinsic enzymes with the function of DOXP synthase, DOXP reductoisomerase or the gcpE protein. This is the case for archaebacteria, animals, fungi, slime moulds and some eubacteria. The absence of such intrinsic enzyme activity substantially facilitates detection and purification of the recombinant enzymes. As a consequence, it is also for the first time possible straightforwardly to measure, in crude extracts from the host cells, the activity and in particular the inhibition of the activity of the recombinant enzymes according to the invention by various chemicals and pharmaceuticals.

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The enzymes according to the invention are advantageously then expressed in eukaryotic cells if post-translational modification and native folding of the polypeptide chain is to be achieved. Moreover, depending upon the expression system, it is ensured when expressing genomic

DNA sequences that introns are eliminated by splicing the DNA and the enzymes are produced in the polypeptide sequences characteristic to the parasites. Using recombinant DNA techniques, sequences coding for introns  
5 may be eliminated from or inserted for experimental purposes into the DNA sequences to be expressed.

The protein may be isolated from the host cell or the culture supernatant of the host cell using methods known  
10 to the person skilled in the art. *In vitro* reactivation of the enzymes may also be required.

In order to facilitate purification, the enzymes according to the invention or sub-sequences of the  
15 enzymes may be expressed as fusion proteins with various peptide chains. Oligo-histidine sequences and sequences derived from glutathione S-transferase, thioredoxin or calmodulin-binding peptides are particularly suitable for this purpose.

The enzymes according to the invention or sub-sequences of the enzymes may furthermore be expressed as fusion proteins with such peptide chains known to the person skilled in the art that the recombinant enzymes are  
20 transported into the extracellular medium or into certain compartments of the host cells. Both purification and investigation of the biological activity of the enzymes  
25 may consequently be facilitated.

When expressing the enzymes according to the invention,  
30 it may prove convenient to modify individual codons. Purposeful replacement of bases in the coding region may here also be advisable if the codons used in the

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parasites differ from the codon use in the heterologous expression system, in order to ensure optimal synthesis of the protein.

5 The enzymes according to the invention may furthermore be obtained under standardised conditions by *in vitro* translation by methods known to the person skilled in the art. Systems suitable for this purpose are rabbit reticulocyte and wheat germ extracts and bacterial  
10 lysates. *In vitro* transcribed mRNA may also be translated into *Xenopus* oocytes.

Oligo- and polypeptides, the sequences of which are derived from the peptide sequence of the enzymes  
15 according to the invention, may be obtained by chemical synthesis. Given appropriate selection of the sequences, such peptides have properties which are characteristic of the enzymes according to the invention. Such peptides may be produced in large quantities and are particularly  
20 suitable for investigating the kinetics of enzyme activity, regulation of enzyme activity, the three-dimensional structure of the enzymes, inhibition of enzyme activity by various chemicals and pharmaceuticals and the binding geometry and binding affinity of various  
25 ligands.

DNA with the nucleotides from sequences SEQ ID no. 1, 3 and 5 are preferably used for the recombinant production of the enzymes according to the invention.

30

The invention accordingly moreover relates to a process for screening for compounds which inhibit the deoxy-D-xylulose phosphate metabolic pathway. According to this

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process, a host organism, which contains a recombinant expression vector, wherein the vector comprises at least a portion of the oligonucleotide sequence according to SEQ ID no. 1, SEQ ID no. 3 or SEQ ID no. 5 or variants or homologues thereof, is provided, as is a compound which is suspected to have antimicrobial, antiparasitic, antibacterial, antiviral and antimycotic action in humans and animals or an antimicrobial, antiviral, bactericidal, herbicidal or fungicidal activity in plants. The host organism is then brought into contact with the compound and the activity of the compound determined.

The present invention also provides methods for determining the enzymatic activity of the gcpE protein. Said activity may be determined using known methods. Determination is performed by detecting the phosphorylation of a sugar or of a phosphorus sugar or of a precursor of isoprenoid biosynthesis, in particular the phosphorylation of 2-C-methyl-D-erythritol, 2-C-methyl-D-erytritol phosphate, in particular 2-C-methyl-D-erythritol 4-phosphate, 2-C-methyl-D-erythrose, 2-C-methyl-D-erythrose phosphate, in particular 2-C-methyl-D-erythrose 4-phosphate. The present invention also provides the use of this measurement method for identifying substances which inhibit the activity of the particular enzymes.

The enzymatic activity of DOXP synthase and DOXP reductoisomerase may be detected in a single step by determining the conversion of glyceraldehyde 3-phosphate into 2-C-methylerythritol 4-phosphate.

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Determination of the activities of DOXP synthase and DOXP reductoisomerase proceeds analogously. Fluorimetric methods described by Querol et al. are also suitable for determining DOXP synthase activity (Querol et al.,  
5 abstracts, 4<sup>th</sup> European Symposium on Plant Isoprenoids, Barcelona, 21-23 April 1999).

T07090-08090860



Claims

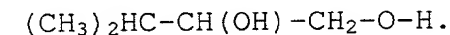
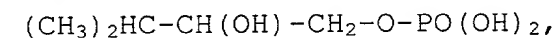
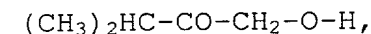
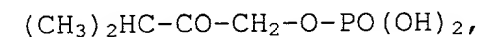
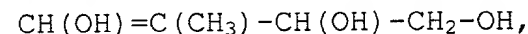
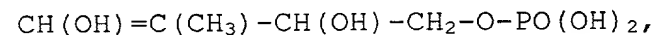
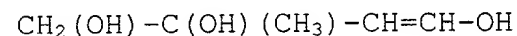
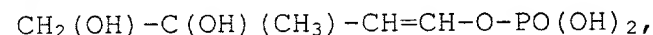
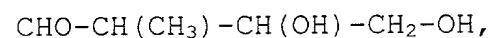
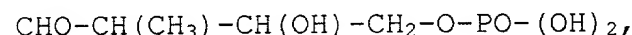
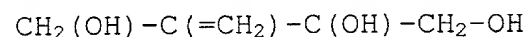
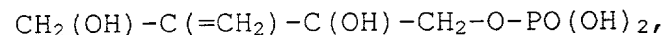
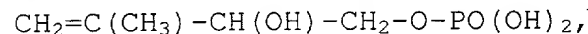
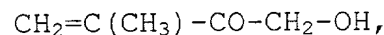
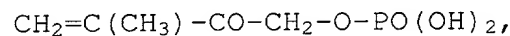
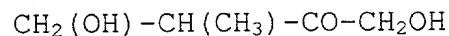
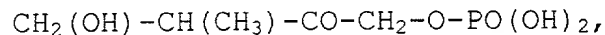
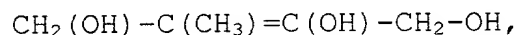
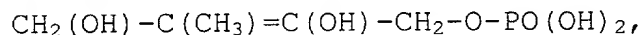
1. DNA sequences which code for a polypeptide with the amino acid sequence shown in SEQ ID no. 2 or for an analogue or derivative of the polypeptide according to SEQ ID no. 2, in which one or more amino acids have been deleted, added or replaced by other amino acids, wherein the enzymatic action of the polypeptide is retained, and which sequences originate from parasites, wherein sequence variations occurring within the framework of natural strain variability are included.
2. DNA sequences which code for a polypeptide with the amino acid sequence shown in SEQ ID no. 4 or for an analogue or derivative of the polypeptide according to SEQ ID no. 4, in which one or more amino acids have been deleted, added or replaced by other amino acids, wherein the enzymatic action of the polypeptide is retained, and which sequences originate from parasites, wherein sequence variations occurring within the framework of natural strain variability are included.
3. DNA sequences which code for a polypeptide with the amino acid sequence shown in SEQ ID no. 6 or for an analogue or derivative of the polypeptide according to SEQ ID no. 6, in which one or more amino acids have been deleted, added or replaced by other amino acids wherein the catalytic function of the polypeptide is retained.

4. DNA sequence according to one of claims 1 to 3, characterised in that it also comprises functional regulation signals, in particular promoters, operators, enhancers, ribosomal binding sites.
- 5
5. DNA sequence with the following sub-sequences
- i) promoter which is active in viruses, eukaryotes and prokaryotes and ensures the formation of an RNA in the intended target tissue or target cells,
  - 10 ii) DNA sequences according to one of claims 1 to 3,
  - iii) 3' untranslated sequence which, in viruses, eukaryotes and prokaryotes, results in the addition of poly(A) residues onto the 3' end of the RNA.
  - 15
6. Process for the production of transgenic viruses, eukaryotes and prokaryotes for modifying the isoprenoid content, characterised in that a DNA sequence according to claim 4 or 5 is transferred and incorporated into the genome of viruses, eukaryotic and prokaryotic cells with or without use of a vector.
- 20
7. Transgenic systems, in particular plants and plant cells which contain one or more DNA sequences according to claims 1 to 5 as "foreign" or "additional" DNA, which sequences are expressed.
- 25
8. Expression vector containing one or more DNA sequences according to claims 1 to 5.
- 30

9. Protein which is involved in the 1-deoxy-D-xylulose 5-phosphate metabolic pathway and a) is coded by DNA sequences SEQ ID no. 1, 3 or 5 or b) is coded by DNA sequences which hybridise with DNA sequences SEQ ID no. 1, 3, 5 or fragments of these DNA sequences in the DNA region which codes for the mature protein.
10. Protein according to claim 9, obtainable from the culture supernatants of parasites or from the disrupted parasites and purification by chromatographic and electrophoretic methods.
11. Protein according to one of claims 9 and 10, characterised in that it a) is the product of viral, prokaryotic or eukaryotic expression of exogenous DNA, b) is coded by sequences SEQ ID no. 1, 3 or 5 or is coded by DNA sequences which hybridise with DNA sequences SEQ ID no. 1, 3, 5 or fragments of these DNA sequences in the DNA region which codes for the mature protein, or c) is coded by DNA sequences which would hybridise without degeneration of the genetic code with the sequences defined in b) and which code for a polypeptide with a corresponding amino acid sequence.
12. Protein according to one of the preceding claims, characterised in that it comprises the amino acid sequences SEQ ID no. 2, 4 or 6.
13. Process for determining the enzymatic activity of the gcpE protein, characterised in that phosphorylation of a sugar or of a phosphorus sugar or of a precursor of isoprenoid biosynthesis, in

particular the phosphorylation of 2-C-methyl-D-erythritol, 2-C-methyl-D-erythritol phosphate, in particular 2-C-methyl-D-erythritol 4-phosphate, 2-C-methyl-D-erythrose, 2-C-methyl-D-erythrose phosphate, in particular 2-C-methyl-D-erythrose 4-phosphate, and of phosphate and alcohol precursors, is detected.

14. Process according to claim 13, characterised in that phosphorylation of the following phosphates or alcohols is detected:



15. Process for the combined determination of the enzymatic activity of DOXP synthase and of DOXP reductase, characterised in that the conversion of glyceraldehyde 3-phosphate into 2-C-methylerythritol 4-phosphate is detected.
16. Process for screening a compound for the treatment of infectious processes in humans and animals, wherein the process comprises:
- a) provision of a host cell which contains a recombinant expression vector, wherein the vector comprises at least a portion of the oligonucleotide sequence according to SEQ ID no. 1, SEQ ID no. 3 or SEQ ID no. 5 or variants or analogues thereof, and moreover of a compound suspected to have antimycotic, antibiotic, antiparasitic or antiviral action in humans and animals,
  - b) bringing the host cell into contact with the compound and
  - c) determining the antimicrobial, antimycotic, antibiotic, antiparasitic or antiviral action of the compound.
17. Process for screening for compounds for treating plants, wherein the process comprises:
- a) provision of a host cell which contains a recombinant expression vector, wherein the vector comprises at least a portion of the oligonucleotide sequence according to SEQ ID no. 1, SEQ ID no. 3 or SEQ ID no. 5 or variants or analogues thereof, and moreover of a compound suspected to have antimicrobial,

- antiviral, antiparasitic, bactericidal,  
fungicidal or herbicidal action in plants,  
b) bringing the host cell into contact with the  
compound and  
5 c) determining the antimicrobial, antiviral,  
antiparasitic, bactericidal, fungicidal or  
herbicidal action of the compound.

- 10 18. Use of DNA according to one of claims 1 to 5 or of  
proteins according to one of claims 9 to 12 or of  
transgenic systems according to claim 7 for the  
prevention or treatment of diseases in humans and  
animals.

09/806080

## SEQUENCE LISTING

&lt;110&gt; Jomaa, Hassan

&lt;120&gt; Genes of the l-decxy-D-xylulose biosynthesis pathway

&lt;130&gt; 15696

&lt;140&gt; PCT/EP99

&lt;141&gt; 1999-09-22

&lt;150&gt; DE19923567.8

&lt;151&gt; 1999-05-22

&lt;150&gt; DE19843279.8

&lt;151&gt; 1998-09-22

&lt;160&gt; 6

&lt;170&gt; PatentIn Ver. 2.1

&lt;210&gt; 1

&lt;211&gt; 1467

&lt;212&gt; DNA

&lt;213&gt; Plasmodium falciparum

&lt;220&gt;

&lt;221&gt; CDS

&lt;222&gt; (1)..(1467)

&lt;220&gt;

&lt;221&gt; gene

&lt;222&gt; (1)..(1467)

&lt;220&gt;

&lt;221&gt; mRNA

&lt;222&gt; (1)..(1467)

&lt;400&gt; 1

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1

5

10

15

aat gat tta gta ata aat aat aca tca aaa tgt gtt tcc att gaa aga 96

Asn Asp Leu Val Ile Asn Asn Thr Ser Lys Cys Val Ser Ile Glu Arg

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25

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aga aaa aat aac gca tat ata aat tat ggt ata gga tat aat gga cca 144

Arg Lys Asn Asn Ala Tyr Ile Asn Tyr Gly Ile Gly Tyr Asn Gly Pro

35

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45

gat aat aaa ata aca aag agt aga aga tgt aaa aga ata aag tta tgc 192

Asp Asn Lys Ile Thr Lys Ser Arg Arg Cys Lys Arg Ile Lys Leu Cys

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60

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- 3 -

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305 310 315 320

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Phe Leu Phe Asp Val Asp Tyr Asn Asp Ile Glu Val Ile Val His Lys  
325 330 335

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370 375 380

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385 390 395 400

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&lt;210&gt; 2

&lt;211&gt; 488

&lt;212&gt; PRT

&lt;213&gt; Plasmodium falciparum

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Asn	Asp	Leu	Val	Ile	Asn	Asn	Thr	Ser	Lys	Cys	Val	Ser	Ile	Glu	Arg
			20					25					30		
Arg	Lys	Asn	Asn	Ala	Tyr	Ile	Asn	Tyr	Gly	Ile	Gly	Tyr	Asn	Gly	Pro
		35					40					45			
Asp	Asn	Lys	Ile	Thr	Lys	Ser	Arg	Arg	Cys	Lys	Arg	Ile	Lys	Leu	Cys
	50					55					60				
Lys	Lys	Asp	Leu	Ile	Asp	Ile	Gly	Ala	Ile	Lys	Lys	Pro	Ile	Asn	Val
65					70					75					80
Ala	Ile	Phe	Gly	Ser	Thr	Gly	Ser	Ile	Gly	Thr	Asn	Ala	Leu	Asn	Ile
				85					90					95	
Ile	Arg	Glu	Cys	Asn	Lys	Ile	Glu	Asn	Val	Phe	Asn	Val	Lys	Ala	Leu
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Tyr	Val	Asn	Lys	Ser	Val	Asn	Glu	Leu	Tyr	Glu	Gln	Ala	Arg	Glu	Phe
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Leu	Pro	Glu	Tyr	Leu	Cys	Ile	His	Asp	Lys	Ser	Val	Tyr	Glu	Glu	Leu
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Gly	Asp	Glu	Gly	Met	Lys	Glu	Ile	Cys	Ser	Ser	Asn	Ser	Ile	Asp	Lys
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Ile	Val	Ile	Gly	Ile	Asp	Ser	Phe	Gln	Gly	Leu	Tyr	Ser	Thr	Met	Tyr
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Ala	Ile	Met	Asn	Asn	Lys	Ile	Val	Ala	Leu	Ala	Asn	Lys	Glu	Ser	Ile
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Val	Ser	Ala	Gly	Phe	Phe	Leu	Lys	Lys	Leu	Leu	Asn	Ile	His	Lys	Asn
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Leu	Asp	Asn	Asn	Lys	Val	Leu	Lys	Thr	Lys	Cys	Leu	Gln	Asp	Asn	Phe
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Ser	Lys	Ile	Asn	Asn	Ile	Asn	Lys	Ile	Phe	Leu	Cys	Ser	Ser	Gly	Gly
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- 6 -

aataatattc taaattttacc ttccgttttt gctcgatctt ctcattttcg tttcagcttt 120  
tatca atg att ttt aat tat gtg ttt ttt aag aac ttt gta cca gtt gtt 170  
Met Ile Phe Asn Tyr Val Phe Phe Lys Asn Phe Val Pro Val Val  
1 5 10 15  
cta tac att ctc ctt ata ata tat att aac tta aat ggc atg aat aat 218  
Leu Tyr Ile Leu Leu Ile Ile Tyr Ile Asn Leu Asn Gly Met Asn Asn  
20 25 30  
aaa aat caa ata aaa aca gaa aaa att tat ata aag aaa ttg aat agg 266  
Lys Asn Gln Ile Lys Thr Glu Lys Ile Tyr Ile Lys Lys Leu Asn Arg  
35 40 45  
ttg tca agg aaa aat tcg tta tgt agt tct aaa aat aaa ata gca tgc 314  
Leu Ser Arg Lys Asn Ser Leu Cys Ser Ser Lys Asn Lys Ile Ala Cys  
50 55 60  
ttg ttc gat ata gga aat gat gat aat aga aat acg aca tat ggc tat 362  
Leu Phe Asp Ile Gly Asn Asp Asp Asn Arg Asn Thr Tyr Gly Tyr  
65 70 75  
aat gtg aat gtt aaa aat gat gat att aat tcc tta cta aaa aat aat 410  
Asn Val Asn Val Lys Asn Asp Asp Ile Asn Ser Leu Leu Lys Asn Asn  
80 85 90 95  
tat agt aat aaa ttg tac atg gat aag agg aaa aat att aat aat gta 458  
Tyr Ser Asn Lys Leu Tyr Met Asp Lys Arg Lys Asn Ile Asn Asn Val  
100 105 110  
att agt act aat aaa ata tot ggg tcc att tca aat att tgt agt aga 506  
Ile Ser Thr Asn Lys Ile Ser Gly Ser Ile Ser Asn Ile Cys Ser Arg  
115 120 125  
aat caa aaa gaa aat gaa caa aaa aga aat aaa caa aga tgt tta act 554  
Asn Gln Lys Glu Asn Glu Gln Lys Arg Asn Lys Gln Arg Cys Leu Thr  
130 135 140  
caa tgt cac act tat aat atg tca cat gaa cag gac aaa cta gct aat 602  
Gln Cys His Thr Tyr Asn Met Ser His Glu Gln Asp Lys Leu Ala Asn  
145 150 155  
gat aat aat agg aat aat aaa aag aat ttt aat tta tta ttt ata aat 650  
Asp Asn Asn Arg Asn Asn Lys Lys Asn Phe Asn Leu Leu Phe Ile Asn  
160 165 170 175  
tat ttt aat ttg aaa cga atg aaa aat tct ctt cta aat aaa gac aat 698  
Tyr Phe Asn Leu Lys Arg Met Lys Asn Ser Leu Leu Asn Lys Asp Asn  
180 185 190  
ttc ttt tac tgt aaa gaa aaa aaa ttg tca ttt ctg cat aag gcc tat 746  
Phe Phe Tyr Cys Lys Glu Lys Lys Leu Ser Phe Leu His Lys Ala Tyr  
195 200 205  
aaa aaa aaa aat tgc act ttt caa aat tat agt tta aaa aga aaa tct 794  
Lys Lys Lys Asn Cys Thr Phe Gln Asn Tyr Ser Leu Lys Arg Lys Ser  
210 215 220

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aat cgt gat tca cat aaa ttg ttt tct gga gaa ttt gac gat tat aca 842  
Asn Arg Asp Ser His Lys Leu Phe Ser Gly Glu Phe Asp Asp Tyr Thr  
225 230 235

aat aat aat gct tta tat gaa tcc gaa aaa aaa gaa tac att aca cta 890  
Asn Asn Asn Ala Leu Tyr Glu Ser Glu Lys Lys Glu Tyr Ile Thr Leu  
240 245 250 255

aat aat aat aat aaa aat aat aat aat aaa aat aat gat aat aaa aat 938  
Asn Asn Asn Asn Lys Asn Asn Asn Asn Lys Asn Asn Asp Asn Lys Asn  
260 265 270

aat gat aat aat gat tat aat aat aat aat agt tgt aat aat tta gga 986  
Asn Asp Asn Asn Asp Tyr Asn Asn Asn Asn Ser Cys Asn Asn Leu Gly  
275 280 285

gag aga tcc aat cat tat gat aat tat ggt gga gat aat aat aat cca 1034  
Glu Arg Ser Asn His Tyr Asp Asn Tyr Gly Gly Asp Asn Asn Asn Pro  
290 295 300

tgt aat aat aat aat gac aaa tat gat ata gga aaa tat ttc aaa cag 1082  
Cys Asn Asn Asn Asn Asp Lys Tyr Asp Ile Gly Lys Tyr Phe Lys Gln  
305 310 315

att aat acc ttt att aat att gat gaa tat aaa act ata tat ggt gat 1130  
Ile Asn Thr Phe Ile Asn Ile Asp Glu Tyr Lys Thr Ile Tyr Gly Asp  
320 325 330 335

gaa ata tat aaa gaa ata tat gaa cta tat gta gaa aga aat att cct 1178  
Glu Ile Tyr Lys Glu Ile Tyr Glu Leu Tyr Val Glu Arg Asn Ile Pro  
340 345 350

gaa tat tat gaa cga aaa tat ttt tca gaa gat att aaa aag agt gtc 1226  
Glu Tyr Tyr Glu Arg Lys Tyr Phe Ser Glu Asp Ile Lys Lys Ser Val  
355 360 365

cta ttt gat ata gat aaa tat aat gat gtc gaa ttt gaa aaa gct ata 1274  
Leu Phe Asp Ile Asp Lys Tyr Asn Asp Val Glu Phe Glu Lys Ala Ile  
370 375 380

aaa gaa gaa ttt ata aat aat gga gtt tat att aat aat ata gat aat 1322  
Lys Glu Glu Phe Ile Asn Asn Gly Val Tyr Ile Asn Asn Ile Asp Asn  
385 390 395

aca tat tat aaa aaa gaa aat att tta ata atg aaa aag ata tta cat 1370  
Thr Tyr Tyr Lys Lys Glu Asn Ile Leu Ile Met Lys Lys Ile Leu His  
400 405 410 415

tat ttc cca tta tta aaa tta att aat aat cca tca gat tta aaa aag 1418  
Tyr Phe Pro Leu Leu Lys Leu Ile Asn Asn Pro Ser Asp Leu Lys Lys  
420 425 430

tta aaa aaa caa tat tta cct tta tta gca cat gaa tta aaa ata ttt 1466  
Leu Lys Lys Gln Tyr Leu Pro Leu Leu Ala His Glu Leu Lys Ile Phe  
435 440 445

09806080 08090860  
TATCCT

tta	ttt	ttt	att	gta	aat	ata	aca	gga	ggg	cat	ttt	tcc	tct	gtt	tta	1514
Leu	Phe	Phe	Ile	Val	Asn	Ile	Thr	Gly	Gly	His	Phe	Ser	Ser	Val	Leu	
		450					455					460				
agc	tct	tta	gaa	att	caa	tta	tta	tta	ttg	tat	att	ttt	aat	caa	cca	1562
Ser	Ser	Leu	Glu	Ile	Gln	Leu	Leu	Leu	Leu	Tyr	Ile	Phe	Asn	Gln	Pro	
		465				470					475					
tat	gat	aat	gtt	ata	tat	gat	ata	gga	cat	caa	gca	tat	gta	cat	aag	1610
Tyr	Asp	Asn	Val	Ile	Tyr	Asp	Ile	Gly	His	Gln	Ala	Tyr	Val	His	Lys	
					485					490					495	
ata	ttg	acc	gga	aga	aaa	cta	tta	ttt	cta	tca	tta	aga	aat	aaa	aaa	1658
Ile	Leu	Thr	Gly	Arg	Lys	Leu	Leu	Phe	Leu	Ser	Leu	Arg	Asn	Lys	Lys	
				500					505					510		
ggg	att	agt	gga	ttc	cta	aat	att	ttt	gaa	agt	att	tat	gat	aaa	ttt	1706
Gly	Ile	Ser	Gly	Phe	Leu	Asn	Ile	Phe	Glu	Ser	Ile	Tyr	Asp	Lys	Phe	
			515					520					525			
ggg	gct	ggg	cac	agt	tcc	act	tca	tta	agt	gct	ata	caa	gga	tat	tat	1754
Gly	Ala	Gly	His	Ser	Ser	Thr	Ser	Leu	Ser	Ala	Ile	Gln	Gly	Tyr	Tyr	
			530				535					540				
gaa	gcc	gag	tggt	caa	gtg	aag	aat	aaa	gaa	aaa	tat	gga	aat	gga	gat	1802
Glu	Ala	Glu	Trp	Gln	Val	Lys	Asn	Lys	Glu	Lys	Tyr	Gly	Asn	Gly	Asp	
						550					555					
ata	gaa	ata	agt	gat	aac	gca	aat	gtc	acg	aat	aat	gaa	agg	ata	ttt	1850
Ile	Glu	Ile	Ser	Asp	Asn	Ala	Asn	Val	Thr	Asn	Asn	Glu	Arg	Ile	Phe	
					565					570					575	
caa	aaa	gga	ata	cac	aat	gat	aat	aat	att	aac	aat	aat	att	aat	aat	1898
Gln	Lys	Gly	Ile	His	Asn	Asp	Asn	Asn	Ile	Asn	Asn	Asn	Ile	Asn	Asn	
				580					585					590		
aat	aat	tat	atc	aat	cct	tca	gat	gtg	gta	gga	aga	gaa	aat	acg	aat	1946
Asn	Asn	Tyr	Ile	Asn	Pro	Ser	Asp	Val	Val	Gly	Arg	Glu	Asn	Thr	Asn	
			595					600					605			
gta	cca	aat	gta	cga	aat	gat	aac	cat	aac	gtg	gat	aaa	gta	cac	att	1994
Val	Pro	Asn	Val	Arg	Asn	Asp	Asn	His	Asn	Val	Asp	Lys	Val	His	Ile	
		610					615					620				
gct	att	ata	gga	gat	ggg	ggg	tta	aca	ggg	gga	atg	gca	tta	gaa	gcg	2042
Ala	Ile	Ile	Gly	Asp	Gly	Gly	Leu	Thr	Gly	Gly	Met	Ala	Leu	Glu	Ala	
						630					635					
tta	aat	tat	att	tca	ttc	ttg	aat	tct	aaa	att	tta	att	att	tat	aat	2090
Leu	Asn	Tyr	Ile	Ser	Phe	Leu	Asn	Ser	Lys	Ile	Leu	Ile	Ile	Tyr	Asn	
					645					650					655	
gat	aac	gga	caa	gtt	tct	tta	cca	aca	aat	gcc	gta	agt	ata	tca	ggg	213

- 9 -

aat aga cct ata ggt tct ata tca gat cat tta cat tat ttt gtt tct	2186
Asn Arg Pro Ile Gly Ser Ile Ser Asp His Leu His Tyr Phe Val Ser	
675 680 685	
aat ata gaa gca aat gct ggt gat aat aaa tta tcg aaa aat gca aaa	2234
Asn Ile Glu Ala Asn Ala Gly Asp Asn Lys Leu Ser Lys Asn Ala Lys	
690 695 700	
gag aat aac att ttt gaa aat ttg aat tat gat tat att ggt gtt gtg	2282
Glu Asn Asn Ile Phe Glu Asn Leu Asn Tyr Asp Tyr Ile Gly Val Val	
705 710 715	
aat ggt aat aat aca gaa gag ctc ttt aaa gta tta aat aat ata aaa	2330
Asn Gly Asn Asn Thr Glu Glu Leu Phe Lys Val Leu Asn Asn Ile Lys	
720 725 730 735	
gaa aat aaa tta aaa aga gct act gtt ctt cat gta cgt aca aaa aaa	2378
Glu Asn Lys Leu Lys Arg Ala Thr Val Leu His Val Arg Thr Lys Lys	
740 745 750	
tcg aat gat ttt ata aat tca aag agt cca ata agt ata ttg cac tct	2426
Ser Asn Asp Phe Ile Asn Ser Lys Ser Pro Ile Ser Ile Leu His Ser	
755 760 765	
ata aag aaa aat gag att ttc cct ttc gat acc act ata tta aat gga	2474
Ile Lys Lys Asn Glu Ile Phe Pro Phe Asp Thr Thr Ile Leu Asn Gly	
770 775 780	
aat att cat aag gag aac aag ata gaa gaa gag aaa aat gtg tct tca	2522
Asn Ile His Lys Glu Asn Lys Ile Glu Glu Glu Lys Asn Val Ser Ser	
785 790 795	
tct aca aag tat gat gta aat aat aag aat aat aaa aat aat gat aat	2570
Ser Thr Lys Tyr Asp Val Asn Asn Lys Asn Asn Lys Asn Asn Asp Asn	
800 805 810 815	
agt gaa att ata aaa tat gaa gat atg ttt tca aaa gag acg ttc aca	2618
Ser Glu Ile Ile Lys Tyr Glu Asp Met Phe Ser Lys Glu Thr Phe Thr	
820 825 830	
gat ata tat aca aat gaa atg tta aaa tat tta aag aaa gat aga aat	2666
Asp Ile Tyr Thr Asn Glu Met Leu Lys Tyr Leu Lys Lys Asp Arg Asn	
835 840 845	
ata ata ttc cta tct ccc gct atg tta gga gga tca gga ttg gtt aaa	2714
Ile Ile Phe Leu Ser Pro Ala Met Leu Gly Gly Ser Gly Leu Val Lys	
850 855 860	
att agt gag cgt tat cca aat aat gta tat gat gta ggt ata gca gaa	2762
Ile Ser Glu Arg Tyr Pro Asn Asn Val Tyr Asp Val Gly Ile Ala Glu	
865 870 875	
caa cat tct gta act ttc gca gca gct atg gca atg aat aag aaa tta	2810
Gln His Ser Val Thr Phe Ala Ala Ala Met Ala Met Asn Lys Lys Leu	
880 885 890 895	

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Ser Thr Asn Lys Ile Ser Gly Ser Ile Ser Asn Ile Cys Ser Arg Asn  
115 120 125

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Gln Lys Glu Asn Glu Gln Lys Arg Asn Lys Gln Arg Cys Leu Thr Gln  
 130 135 140  
 Cys His Thr Tyr Asn Met Ser His Glu Gln Asp Lys Leu Ala Asn Asp  
 145 150 155 160  
 Asn Asn Arg Asn Asn Lys Lys Asn Phe Asn Leu Leu Phe Ile Asn Tyr  
 165 170 175  
 Phe Asn Leu Lys Arg Met Lys Asn Ser Leu Leu Asn Lys Asp Asn Phe  
 180 185 190  
 Phe Tyr Cys Lys Glu Lys Lys Leu Ser Phe Leu His Lys Ala Tyr Lys  
 195 200 205  
 Lys Lys Asn Cys Thr Phe Gln Asn Tyr Ser Leu Lys Arg Lys Ser Asn  
 210 215 220  
 Arg Asp Ser His Lys Leu Phe Ser Gly Glu Phe Asp Asp Tyr Thr Asn  
 225 230 235 240  
 Asn Asn Ala Leu Tyr Glu Ser Glu Lys Lys Glu Tyr Ile Thr Leu Asn  
 245 250 255  
 Asn Asn Asn Lys Asn Asn Asn Asn Lys Asn Asn Asp Asn Lys Asn Asn  
 260 265 270  
 Asp Asn Asn Asp Tyr Asn Asn Asn Asn Ser Cys Asn Asn Leu Gly Glu  
 275 280 285  
 Arg Ser Asn His Tyr Asp Asn Tyr Gly Gly Asp Asn Asn Asn Pro Cys  
 290 295 300  
 Asn Asn Asn Asn Asp Lys Tyr Asp Ile Gly Lys Tyr Phe Lys Gln Ile  
 305 310 315 320  
 Asn Thr Phe Ile Asn Ile Asp Glu Tyr Lys Thr Ile Tyr Gly Asp Glu  
 325 330 335  
 Ile Tyr Lys Glu Ile Tyr Glu Leu Tyr Val Glu Arg Asn Ile Pro Glu  
 340 345 350  
 Tyr Tyr Glu Arg Lys Tyr Phe Ser Glu Asp Ile Lys Lys Ser Val Leu  
 355 360 365  
 Phe Asp Ile Asp Lys Tyr Asn Asp Val Glu Phe Glu Lys Ala Ile Lys  
 370 375 380  
 Glu Glu Phe Ile Asn Asn Gly Val Tyr Ile Asn Asn Ile Asp Asn Thr  
 385 390 395 400  
 Tyr Tyr Lys Lys Glu Asn Ile Leu Ile Met Lys Lys Ile Leu His Tyr  
 405 410 415  
 Phe Pro Leu Leu Lys Leu Ile Asn Asn Pro Ser Asp Leu Lys Lys Leu  
 420 425 430

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 090006080.060404

Lys	Lys	Gln	Tyr	Leu	Pro	Leu	Leu	Ala	His	Glu	Leu	Lys	Ile	Phe	Leu
		435					440					445			
Phe	Phe	Ile	Val	Asn	Ile	Thr	Gly	Gly	His	Phe	Ser	Ser	Val	Leu	Ser
	450					455					460				
Ser	Leu	Glu	Ile	Gln	Leu	Leu	Leu	Leu	Tyr	Ile	Phe	Asn	Gln	Pro	Tyr
465					470					475					480
Asp	Asn	Val	Ile	Tyr	Asp	Ile	Gly	His	Gln	Ala	Tyr	Val	His	Lys	Ile
				485					490					495	
Leu	Thr	Gly	Arg	Lys	Leu	Leu	Phe	Leu	Ser	Leu	Arg	Asn	Lys	Lys	Gly
			500					505					510		
Ile	Ser	Gly	Phe	Leu	Asn	Ile	Phe	Glu	Ser	Ile	Tyr	Asp	Lys	Phe	Gly
		515					520					525			
Ala	Gly	His	Ser	Ser	Thr	Ser	Leu	Ser	Ala	Ile	Gln	Gly	Tyr	Tyr	Glu
	530					535					540				
Ala	Glu	Trp	Gln	Val	Lys	Asn	Lys	Glu	Lys	Tyr	Gly	Asn	Gly	Asp	Ile
545					550					555					560
Glu	Ile	Ser	Asp	Asn	Ala	Asn	Val	Thr	Asn	Asn	Glu	Arg	Ile	Phe	Gln
				565					570					575	
Lys	Gly	Ile	His	Asn	Asp	Asn	Asn	Ile	Asn	Asn	Asn	Ile	Asn	Asn	Asn
			580					585					590		
Asn	Tyr	Ile	Asn	Pro	Ser	Asp	Val	Val	Gly	Arg	Glu	Asn	Thr	Asn	Val
		595					600					605			
Pro	Asn	Val	Arg	Asn	Asp	Asn	His	Asn	Val	Asp	Lys	Val	His	Ile	Ala
	610					615					620				
Ile	Ile	Gly	Asp	Gly	Gly	Leu	Thr	Gly	Gly	Met	Ala	Leu	Glu	Ala	Leu
625					630					635					640
Asn	Tyr	Ile	Ser	Phe	Leu	Asn	Ser	Lys	Ile	Leu	Ile	Ile	Tyr	Asn	Asp
				645					650					655	
Asn	Gly	Gln	Val	Ser	Leu	Pro	Thr	Asn	Ala	Val	Ser	Ile	Ser	Gly	Asn
			660					665					670		
Arg	Pro	Ile	Gly	Ser	Ile	Ser	Asp	His	Leu	His	Tyr	Phe	Val	Ser	Asn
		675					680					685			
Ile	Glu	Ala	Asn	Ala	Gly	Asp	Asn	Lys	Leu	Ser	Lys	Asn	Ala	Lys	Glu
	690					695					700				
Asn	Asn	Ile	Phe	Glu	Asn	Leu	Asn	Tyr	Asp	Tyr	Ile	Gly	Val	Val	Asn
705					710					715					720
Gly	Asn	Asn	Thr	Glu	Glu	Leu	Phe	Lys	Val	Leu	Asn	Asn	Ile	Lys	Glu
				725					730					735	

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Asn	Lys	Leu	Lys	Arg	Ala	Thr	Val	Leu	His	Val	Arg	Thr	Lys	Lys	Ser	
			740					745					750			
Asn	Asp	Phe	Ile	Asn	Ser	Lys	Ser	Pro	Ile	Ser	Ile	Leu	His	Ser	Ile	
		755					760					765				
Lys	Lys	Asn	Glu	Ile	Phe	Pro	Phe	Asp	Thr	Thr	Ile	Leu	Asn	Gly	Asn	
		770				775					780					
Ile	His	Lys	Glu	Asn	Lys	Ile	Glu	Glu	Glu	Lys	Asn	Val	Ser	Ser	Ser	
785					790					795						800
Thr	Lys	Tyr	Asp	Val	Asn	Asn	Lys	Asn	Asn	Lys	Asn	Asn	Asp	Asn	Ser	
				805					810					815		
Glu	Ile	Ile	Lys	Tyr	Glu	Asp	Met	Phe	Ser	Lys	Glu	Thr	Phe	Thr	Asp	
			820					825					830			
Ile	Tyr	Thr	Asn	Glu	Met	Leu	Lys	Tyr	Leu	Lys	Lys	Asp	Arg	Asn	Ile	
		835					840					845				
Ile	Phe	Leu	Ser	Pro	Ala	Met	Leu	Gly	Gly	Ser	Gly	Leu	Val	Lys	Ile	
	850					855					860					
Ser	Glu	Arg	Tyr	Pro	Asn	Asn	Val	Tyr	Asp	Val	Gly	Ile	Ala	Glu	Gln	
865					870					875					880	
His	Ser	Val	Thr	Phe	Ala	Ala	Ala	Met	Ala	Met	Asn	Lys	Lys	Leu	Lys	
				885					890					895		
Ile	Gln	Leu	Cys	Ile	Tyr	Ser	Thr	Phe	Leu	Gln	Arg	Ala	Tyr	Asp	Gln	
			900					905					910			
Ile	Ile	His	Asp	Leu	Asn	Leu	Gln	Asn	Ile	Pro	Leu	Lys	Val	Ile	Ile	
		915					920					925				
Gly	Arg	Ser	Gly	Leu	Val	Gly	Glu	Asp	Gly	Ala	Thr	His	Gln	Gly	Ile	
	930					935					940					
Tyr	Asp	Leu	Ser	Tyr	Leu	Gly	Thr	Leu	Asn	Asn	Ala	Tyr	Ile	Ile	Ser	
945					950					955					960	
Pro	Ser	Asn	Gln	Val	Asp	Leu	Lys	Arg	Ala	Leu	Arg	Phe	Ala	Tyr	Leu	
				965					970					975		
Asp	Lys	Asp	His	Ser	Val	Tyr	Ile	Arg	Ile	Pro	Arg	Met	Asn	Ile	Leu	
			980					985					990			
Ser	Asp	Lys	Tyr	Met	Lys	Gly	Tyr	Leu	Asn	Ile	His	Met	Lys	Asn	Glu	
		995					1000					1005				
Ser	Lys	Asn	Ile	Asp	Val	Asn	Val	Asp	Ile	Asn	Asp	Asp	Val	Asp	Lys	
	1010					1015					1020					
Tyr	Ser	Glu	Glu	Tyr	Met	Asp	Asp	Asp	Asn	Phe	Ile	Lys	Ser	Phe	Ile	
025					1030					1035					1040	

tta ctg ttt tat tct cat gta aaa att aaa aaa tta ttt att aaa att 279  
Leu Leu Phe Tyr Ser His Val Lys Ile Lys Lys Leu Phe Ile Lys Ile  
15 20 25

- 16 -

tct aat gta aac ata ttt ttt gca gaa gca aag aaa aat gga aaa aag 327  
Ser Asn Val Asn Ile Phe Phe Ala Glu Ala Lys Lys Asn Gly Lys Lys  
30 35 40

gaa ttc ttt ctt ttt tta cta aat ata aaa aaa aat agc caa cag aaa 375  
Glu Phe Phe Leu Phe Leu Leu Asn Ile Lys Lys Asn Ser Gln Gln Lys  
45 50 55

aaa act tat cat att acc aaa agg aat acc ata aat aaa agt gat ttt 423  
Lys Thr Tyr His Ile Thr Lys Arg Asn Thr Ile Asn Lys Ser Asp Phe  
60 65 70 75

tta tat tct tta cta aat gaa gaa ggg aat tct tca aaa aag gaa tat 471  
Leu Tyr Ser Leu Leu Asn Glu Glu Gly Asn Ser Ser Lys Lys Glu Tyr  
80 85 90

aaa aat tta aaa gat gaa gaa aaa tat aat atc ata caa aat ata aaa 519  
Lys Asn Leu Lys Asp Glu Glu Lys Tyr Asn Ile Ile Gln Asn Ile Lys  
95 100 105

aaa tat tgt gaa tgt act aaa aaa tat aaa agg ctc cca aca cga gaa 567  
Lys Tyr Cys Glu Cys Thr Lys Lys Tyr Lys Arg Leu Pro Thr Arg Glu  
110 115 120

gta gtt att gga aat gtt aaa att gga gga aat aat aaa ata gct att 615  
Val Val Ile Gly Asn Val Lys Ile Gly Gly Asn Asn Lys Ile Ala Ile  
125 130 135

caa act atg gct agc tgt gat aca aga aat gta gaa gaa tgt gta tat 663  
Gln Thr Met Ala Ser Cys Asp Thr Arg Asn Val Glu Glu Cys Val Tyr  
140 145 150 155

caa att aga aaa tgt aaa gat ttg ggt gct gac att gta agg ttg act 711  
Gln Ile Arg Lys Cys Lys Asp Leu Gly Ala Asp Ile Val Arg Leu Thr  
160 165 170

gtt caa gga gtt caa gaa gca caa gct agt tat cat att aaa gaa aaa 759  
Val Gln Gly Val Gln Glu Ala Gln Ala Ser Tyr His Ile Lys Glu Lys  
175 180 185

tta tta tct gaa aat gta aat atc cca tta gta gca gat att cat ttt 807  
Leu Leu Ser Glu Asn Val Asn Ile Pro Leu Val Ala Asp Ile His Phe  
190 195 200

aat cct aaa ata gct tta atg gca gct gat gtg ttt gaa aaa att cga 855  
Asn Pro Lys Ile Ala Leu Met Ala Ala Asp Val Phe Glu Lys Ile Arg  
205 210 215

gtg aat cca gga aat tat gtt gat gga aga aaa aaa tgg ata gat aaa 903  
Val Asn Pro Gly Asn Tyr Val Asp Gly Arg Lys Lys Trp Ile Asp Lys  
220 225 230 235

gtt tat aaa aat aaa gaa gaa ttt gat gaa ggg aaa tta ttt ata aaa 951  
Val Tyr Lys Thr Lys Glu Glu Phe Asp Glu Gly Lys Leu Phe Ile Lys  
240 245 250









His	Val	Lys	Ile	Lys	Lys	Leu	Phe	Ile	Lys	Ile	Ser	Asn	Val	Asn	Ile
			20					25					30		
Phe	Phe	Ala	Glu	Ala	Lys	Lys	Asn	Gly	Lys	Lys	Glu	Phe	Phe	Leu	Phe
		35					40					45			
Leu	Leu	Asn	Ile	Lys	Lys	Asn	Ser	Gln	Gln	Lys	Lys	Thr	Tyr	His	Ile
	50					55					60				
Thr	Lys	Arg	Asn	Thr	Ile	Asn	Lys	Ser	Asp	Phe	Leu	Tyr	Ser	Leu	Leu
65					70					75					80
Asn	Glu	Glu	Gly	Asn	Ser	Ser	Lys	Lys	Glu	Tyr	Lys	Asn	Leu	Lys	Asp
				85					90					95	
Glu	Glu	Lys	Tyr	Asn	Ile	Ile	Gln	Asn	Ile	Lys	Lys	Tyr	Cys	Glu	Cys
			100					105					110		
Thr	Lys	Lys	Tyr	Lys	Arg	Leu	Pro	Thr	Arg	Glu	Val	Val	Ile	Gly	Asn
		115					120					125			
Val	Lys	Ile	Gly	Gly	Asn	Asn	Lys	Ile	Ala	Ile	Gln	Thr	Met	Ala	Ser
	130					135					140				
Cys	Asp	Thr	Arg	Asn	Val	Glu	Glu	Cys	Val	Tyr	Gln	Ile	Arg	Lys	Cys
145					150					155					160
Lys	Asp	Leu	Gly	Ala	Asp	Ile	Val	Arg	Leu	Thr	Val	Gln	Gly	Val	Gln
				165					170					175	
Glu	Ala	Gln	Ala	Ser	Tyr	His	Ile	Lys	Glu	Lys	Leu	Leu	Ser	Glu	Asn
			180					185					190		
Val	Asn	Ile	Pro	Leu	Val	Ala	Asp	Ile	His	Phe	Asn	Pro	Lys	Ile	Ala
		195					200					205			
Leu	Met	Ala	Ala	Asp	Val	Phe	Glu	Lys	Ile	Arg	Val	Asn	Pro	Gly	Asn
	210					215					220				
Tyr	Val	Asp	Gly	Arg	Lys	Lys	Trp	Ile	Asp	Lys	Val	Tyr	Lys	Thr	Lys
225					230					235					240
Glu	Glu	Phe	Asp	Glu	Gly	Lys	Leu	Phe	Ile	Lys	Glu	Lys	Phe	Val	Pro
				245					250					255	
Leu	Ile	Glu	Lys	Cys	Lys	Arg	Leu	Asn	Arg	Ala	Ile	Arg	Ile	Gly	Thr
			260					265					270		
Asn	His	Gly	Ser	Leu	Ser	Ser	Arg	Val	Leu	Ser	Tyr	Tyr	Gly	Asp	Thr
		275					280					285			
Pro	Leu	Gly	Met	Val	Glu	Ser	Ala	Phe	Glu	Phe	Ser	Asp	Leu	Cys	Ile
						295						300			
Glu	Asn	Asn	Phe	Tyr	Asn	Leu	Val	Phe	Ser	Met	Lys	Ala	Ser	Asn	Ala
305					310					315					320
Tyr	Val	Met	Ile	Gln	Ser	Tyr	Arg	Leu	Leu	Val	Ser	Lys	Gln	Tyr	Gln

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325 330 335  
 Arg Asn Met Met Phe Pro Ile His Leu Gly Val Thr Glu Ala Gly Phe  
 340 345 350  
 Gly Asp Asn Gly Arg Ile Lys Ser Tyr Leu Gly Ile Gly Ser Leu Leu  
 355 360 365  
 Tyr Asp Gly Ile Gly Asp Thr Ile Arg Ile Ser Leu Thr Glu Asp Pro  
 370 375 380  
 Trp Glu Glu Leu Thr Pro Cys Lys Lys Leu Val Glu Asn Leu Lys Lys  
 385 390 395 400  
 Arg Ile Phe Tyr Asn Glu Asn Phe Lys Glu Asp Asn Glu Leu Lys Asn  
 405 410 415  
 Asn Glu Met Asp Thr Lys Asn Leu Leu Asn Phe Glu Glu Asn Tyr Arg  
 420 425 430  
 Asn Phe Asn Asn Ile Lys Lys Arg Asn Val Glu Lys Asn Asn Asn Val  
 435 440 445  
 Leu His Glu Glu Cys Thr Ile Gly Asn Val Val Thr Ile Lys Glu Leu  
 450 455 460  
 Glu Asp Ser Leu Gln Ile Phe Lys Asp Leu Asn Leu Glu Val Asp Ser  
 465 470 475 480  
 Asn Gly Asn Leu Lys Lys Gly Ala Lys Thr Thr Asp Met Val Ile Ile  
 485 490 495  
 Asn Asp Phe His Asn Ile Thr Asn Leu Gly Lys Lys Thr Val Asp Lys  
 500 505 510  
 Leu Met Gln Val Gly Ile Asn Ile Val Val Gln Tyr Glu Pro His Asn  
 515 520 525  
 Ile Glu Phe Ile Glu Lys Met Glu Pro Asn Asn Asp Asn Asn Asn Asn  
 530 535 540  
 Asn Asn Asn Asn Asn Ile Leu Phe Tyr Val Asp Ile Lys Asn Ile Met  
 545 550 555 560  
 Asn Ser Ser Glu Lys Asn Ile Lys Leu Ser Asn Ser Lys Gly Tyr Gly  
 565 570 575  
 Leu Ile Leu Asn Gly Lys Glu Asp Ile Gln Thr Ile Lys Lys Ile Lys  
 580 585 590  
 Glu Leu Asn Arg Arg Pro Leu Phe Ile Leu Leu Lys Ser Asp Asn Ile  
 595 600 605  
 Tyr Glu His Val Leu Ile Thr Arg Arg Ile Asn Glu Leu Leu Gln Ser  
 610 615 620  
 Leu Asn Ile Asn Ile Pro Tyr Ile His Tyr Val Asp Ile Asn Ser Asn  
 625 630 635 640

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Asn Tyr Asp Asp Ile Leu Val Asn Ser Thr Leu Tyr Ala Gly Ser Cys  
 645 650 655  
 Leu Met Asp Leu Met Gly Asp Gly Leu Ile Val Asn Val Thr Asn Asp  
 660 665 670  
 Val Leu Thr Asn Lys Lys Lys Ile Glu Thr Lys Tyr Asp Glu Lys Glu  
 675 680 685  
 Glu Val Glu Glu Glu Gly Asn Asn Lys Asp Ile His Arg Leu Leu Ser  
 690 695 700  
 Arg Val Ala Leu Asn Ser Phe Leu Thr Leu Asn Ile Leu Gln Asp Thr  
 705 710 715 720  
 Arg Ile Arg Leu Phe Lys Thr Asp Tyr Ile Ala Cys Pro Ser Cys Gly  
 725 730 735  
 Arg Thr Leu Phe Asn Ile Gln Glu Thr Thr Lys Lys Ile Met Lys Leu  
 740 745 750  
 Thr Gly His Leu Lys Gly Val Lys Ile Ala Val Met Gly Cys Ile Val  
 755 760 765  
 Asn Gly Ile Gly Glu Met Ala Asp Ala His Phe Gly Tyr Val Gly Ser  
 770 775 780  
 Ala Pro Lys Lys Ile Asp Leu Tyr Tyr Gly Lys Glu Leu Val Glu Arg  
 785 790 795 800  
 Asn Ile Pro Glu Glu Glu Ala Cys Asp Lys Leu Ile Glu Leu Ile Lys  
 805 810 815  
 Lys His Asn Lys Trp Lys Asp Pro  
 820

# Declaration and Power of Attorney for Patent Application

## Erklärung für Patentanmeldungen mit Vollmacht

### German Language Declaration

Als nachstehend benannter Erfinder erkläre ich hiermit an Eides Statt:

daß mein Wohnsitz, meine Postanschrift und meine Staatsangehörigkeit den im nachstehenden nach meinem Namen aufgeführten Angaben entsprechen, daß ich nach bestem Wissen der ursprüngliche, erste und alleinige Erfinder (falls nachstehend nur ein Name angegeben ist) oder ein ursprünglicher, erster und Miterfinder (falls nachstehend mehrere Namen aufgeführt sind) des Gegenstandes bin, für den dieser Antrag gestellt wird und für den ein Patent für die Erfindung mit folgendem Titel beantragt wird:

\_\_\_\_\_

\_\_\_\_\_

deren Beschreibung hier beigelegt ist, es sei denn (in diesem Falle Zutreffendes bitte ankreuzen), diese Erfindung

- ☐ wurde angemeldet am \_\_\_\_\_ unter der US-Anmeldenummer oder unter der Internationalen Anmeldenummer im Rahmen des Vertrags über die Zusammenarbeit auf dem Gebiet des Patentwesens (PCT) \_\_\_\_\_ und am \_\_\_\_\_ abgeändert (falls zutreffend).

Ich bestätige hiermit, daß ich den Inhalt der oben angegebenen Patentanmeldung, einschließlich der Ansprüche, die eventuell durch einen oben erwähnten Zusatzantrag abgeändert wurde, durchgesehen und verstanden habe.

Ich erkenne meine Pflicht zur Offenbarung jeglicher Informationen an, die zur Prüfung der Patentfähigkeit in Einklang mit Titel 37, Code of Federal Regulations, § 1.56 von Belang sind.

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled

\_\_\_\_\_

\_\_\_\_\_

the specification of which is attached hereto unless the following box is checked:

- ☐ was filed on \_\_\_\_\_ as United States Application Number or PCT International Application Number \_\_\_\_\_ and was amended on \_\_\_\_\_ (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, § 1.56.

## German Language Declaration

Ich beanspruche hiermit ausländische Prioritätsvorteile gemäß Title 35, US-Code, § 119 (a)-(d), bzw. § 365(b) aller unten aufgeführten Auslandsanmeldungen für Patente oder Erfinderurkunden, oder § 365(a) aller PCT internationalen Anmeldungen, welche wenigstens ein Land ausser den Vereinigten Staaten von Amerika benennen, und habe nachstehend durch ankreuzen sämtliche Auslandsanmeldungen für Patente bzw. Erfinderurkunden oder PCT internationale Anmeldungen angegeben, deren Anmeldetag dem der Anmeldung, für welche Priorität beansprucht wird, vorangeht.

**Prior Foreign Applications**  
(Frühere ausländische Anmeldungen)

Priority Not Claimed  
Priorität nicht beansprucht

(Number)	<b>Germany</b>
(Nummer)	(Country)
	(Land)

(Day/Month/Year Filed)  
(Tag/Monat/Jahr der Anmeldung)

(Number)	Germany
(Nummer)	(Country)
	(Land)

(Day/Month/Year Filed)  
(Tag/Monat/Jahr der Anmeldung)

Ich beanspruche hiermit Prioritätsvorteile unter Title 35, US-Code, § 119(e) aller US-Hilfsanmeldungen wie unten aufgezählt.

I hereby claim the benefit under Title 35, United States Code,  
§ 119(e) of any United States provisional application(s) listed below.

(Application No.)	(Filing Date)
(Aktenzeichen)	(Anmeldetag)

(Application No.)	(Filing Date)
(Aktenzeichen)	(Anmeldetag)

Ich beanspruche hiermit die mir unter Title 35, US-Code, § 120 zustehenden Vorteile aller unten aufgeführten US-Patentanmeldungen bzw. § 365(c) aller PCT internationalen Anmeldungen, welche die Vereinigten Staaten von Amerika benennen, und erkenne, insofern der Gegenstand eines jeden früheren Anspruchs dieser Patentanmeldung nicht in einer US-Patentanmeldung, bzw. PCT internationalen Anmeldung in einer gemäß dem ersten Absatz von Title 35, US-Code, § 112 vorgeschriebenen Art und Weise offenbart wurde, meine Pflicht zur Offenbarung jeglicher Informationen an, die zur Prüfung der Patentfähigkeit in Einklang mit Title 37, Code of Federal Regulations, § 1.56 von Belang sind und die im Zeitraum zwischen dem Anmeldetag der früheren Patentanmeldung und dem nationalen oder im Rahmen des Vertrags über die Zusammenarbeit auf dem Gebiet des Patentwesens (PCT) gültigen internationalen Anmeldetags bekannt geworden sind.

I hereby claim the benefit under Title 35, United States Code, § 120 of any United States application(s), or § 365(c) of any PCT International application designating the United States, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of Title 35, United States Code, § 112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, § 1.56 which became available between the filing date of the prior application and the national or PCT International filing date of this application.

(Application No.)	(Filing Date)
(Aktenzeichen)	(Anmeldetag)

Pending  
(Status) (patented, pending, abandoned)  
(Status) (patentiert, schwebend, aufgegeben)

(Application No.)	(Filing Date)
(Aktenzeichen)	(Anmeldetag)

(Status) (patented, pending, abandoned)  
(Status) (patentiert, schwebend, aufgegeben)

Ich erkläre hiermit, daß alle in der vorliegenden Erklärung von mir gemachten Angaben nach bestem Wissen und Gewissen der Wahrheit entsprechen, und ferner daß ich diese eidesstattliche Erklärung in Kenntnis dessen ablege, daß wissenschaftlich und vorsätzlich falsche Angaben oder dergleichen gemäß § 1001, Title 18 des US-Code strafbar sind und mit Geldstrafe und/oder Gefängnis bestraft werden können und daß derartige wissenschaftlich und vorsätzlich falsche Angaben die Rechtswirksamkeit der vorliegenden Patentanmeldung oder eines auf deren erteilten Patentes gefährden können.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

### German Language Declaration

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Postanschrift:

Telefonische Auskünfte: (Name und Telefonnummer)

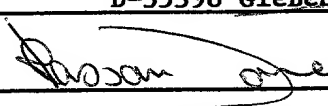
POWER OF ATTORNEY: As a named inventor, I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith: (list name and registration number)

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Vor- und Zuname des einzigen oder ersten Erfinders	Full name of sole or first inventor <b>Hassan Jomaa</b>
Unterschrift des Erfinders Datum	Inventor's signature Date <b>28/02/07</b>
Wohnsitz	Residence <b>Breslauer Strasse 24 D-35398 Gießen, Germany</b>
Staatsangehörigkeit	Citizenship <b>Germany</b>
Postanschrift	Post Office Address <b>Breslauer Strasse 24 D-35398 Gießen, Germany</b>
	
Vor- und Zuname des zweiten Miterfinders (falls zutreffend)	Full name of second joint inventor, if any
Unterschrift des zweiten Erfinders Datum	Second Inventor's signature Date
Wohnsitz	Residence
Staatsangehörigkeit	Citizenship
Postanschrift	Post Office Address

(Im Falle dritter und weiterer Miterfinder sind die entsprechenden Informationen und Unterschriften hinzuzufügen.)

(Supply similar information and signature for third and subsequent joint inventors.)